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# THE CENTRAL NERVOUS SYSTEM AND BEHAVIOR

*Transactions of the Third Conference*
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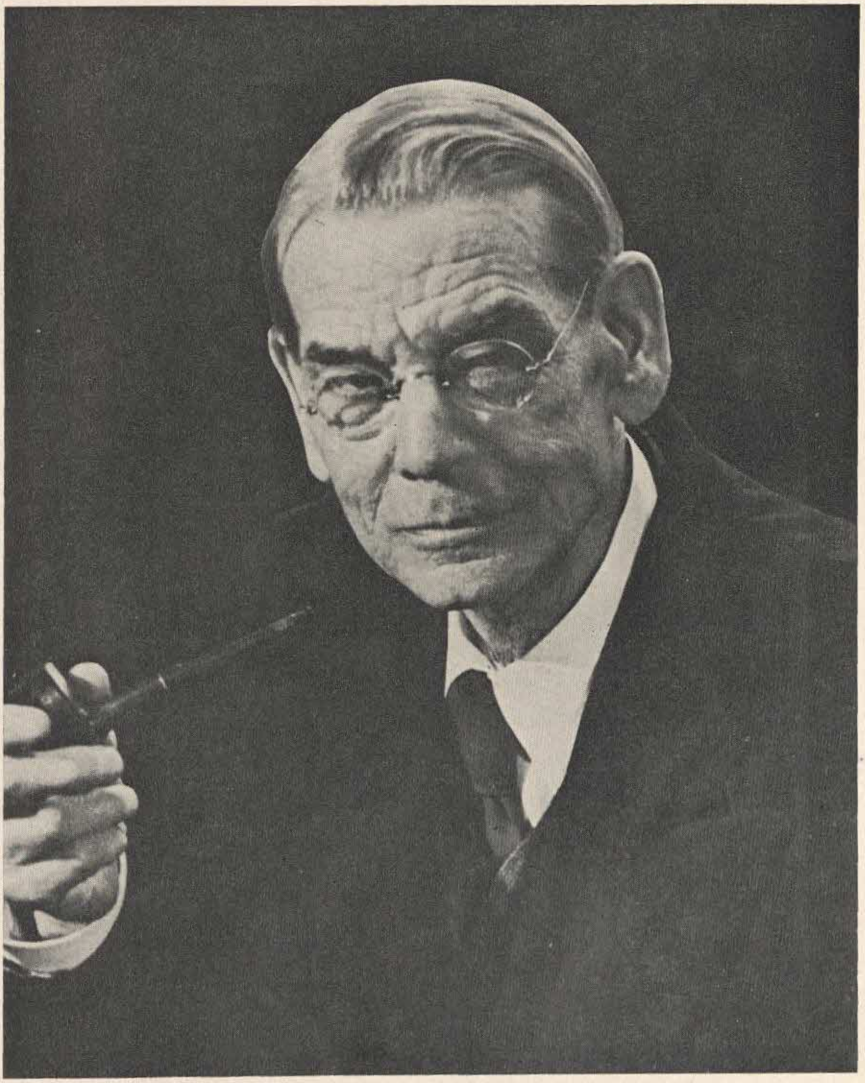

C. JUDSON HERRICK (1868-1960)

"Our mode of life has been achieved through eons of evolutionary change, during which the conservative and relatively stable organization of the brain stem has been supplemented and amplified by the addition of cortical apparatus with more labile patterns of action, resulting in greater freedom of adjustment to the exigencies of life. In all behavior there is a substrate of innate patterns of great antiquity, and in practical adjustments these primitive factors are manipulated and recombined in terms of the individual's personal experience. Memory and learning are pre-eminently cortical functions, but these cortical capacities have not been given to us by magic, and we want to know how they have been developed and the roots from which they have grown." Reprinted from Herrick, C. J.: *The Brain of the Tiger Salamander, Ambystoma tigrinum*. Chicago, University of Chicago Press, 1948, p. 122.

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# THE JOSIAH MACY, JR. FOUNDATION CONFERENCE PROGRAM

During the past fifteen years the Josiah Macy, Jr. Foundation has organized more than twenty conference groups, each group meeting for at least two days annually over a period of five or more years. Each meeting is limited to twenty-five participants (members and guests), selected to represent a multidisciplinary approach to some urgent problem in the field of medicine and health. The goal of this conference program is the promotion of communication, the exchange of ideas, and the stimulation of creativity among the participants. The purpose of the publication of the Transactions of the meetings is to share, as far as possible, the conference process with a larger audience than could participate personally in the discussions.

These conferences provide an opportunity for informal give and take among the participants. To further this purpose, the number of presentations planned for each day is generally restricted to one or two. The members, or guests, selected to give such a presentation are requested not to "read a paper," but rather to highlight, in an informal manner, some of the more interesting aspects of their research, with the expectation that there will be frequent interruptions by participants in the form of questions, criticism, or comment. Such interruptions during the course of a presentation are encouraged and form an essential part of the "group interchange."

The conference program has always been viewed by the Foundation as an experiment in communication in which there is room for improvement and need for frequent reappraisal. Sufficient experience has already been gained to justify the conclusion that this type of conference is an effective way of improving understanding among scientists in medicine and allied disciplines, for broadening perspectives, for changing attitudes, and for overcoming prejudices. The further conclusion has been reached, as the result of this experiment, that a major obstruction to understanding among scientists lies in the resistance of human attitudes to change, rather than in difficulties of technical comprehension. Less extensive experience with non-scientists has indicated that the effectiveness of this type of conference is not limited to groups of scientists, but will function in any group meeting where more effective communication is the primary goal. It is also clear that the same conference technique, with minor changes, is readily adaptable to small international conferences.

The style of publication of the Transactions has aroused considerable interest and some criticism. The criticism has been directed primarily to editorial permissiveness which has allowed in the final text, in some instances, too many questions, remarks, or comments which, although perhaps useful during a heated discussion, seem out of context and interrupt the sequence of thought. A few have objected to the principle of publishing in this style and would prefer a depersonalized summary without interruptions.

FRANK FREMONT-SMITH, M.D.
*Medical Director*

# INTRODUCTORY REMARKS

*Magoun:* This conference on The Central Nervous System and Behavior follows the pattern of the previous Macy Conferences established under the leadership of Dr. Frank Fremont-Smith in that it is multidisciplinary in scope and international in participation. Characteristically, too, it is concerned with a topic currently of major interest. The increasingly intimate relationship between brain function and behavior seems almost as spectacular in biology and medicine today as that of mass and energy in the physical sciences.

One of the most fruitful approaches to the study of brain activity and behavior has been that of conditional reflex physiology, begun early in the century by I. P. Pavlov in Russia. This objective study of "higher nervous activity" has since been extended widely by Pavlov's successors both in the USSR and in the Peoples' Democracies of Eastern Europe, but Western scientists have remained regrettably uninformed of their accomplishments. In the programming of this conference series, a special effort has been made to consider these developments along with those that have been made in the West. In line with this, the support of the National Science Foundation has made possible both translations of publications from the Russian language and the participation of Soviet and Eastern European scientists at these meetings, for which the members of the conference are most appreciative.

Each of the three conferences in this series has been devoted to a special aspect of the Central Nervous System and Behavior. The first, in 1958, surveyed the rise of Russian science through the Pavlovian period, and then explored current investigations of conditional reflexes that have been carried on in this country, in particular, those with the techniques of electrophysiology. The second conference, in 1959, was devoted to a consideration of the emotional and motivational mechanisms of the brain and enjoyed the participation from abroad of Dr. H. C. Rümke from Holland, Dr. Jan Bureš from Czechoslovakia, Dr. Endre Grastyán from Hungary, and Professor Vladimir Sergeivich Rusinov from the USSR.

The present conference has as its theme the maturation of the central nervous system and behavior. It is a special pleasure for me to welcome participants both from home and from abroad. Among the latter are included Dr. Robert A. Hinde, from England, and Professor Eugene

Nikolaievich Sokolov and Professor Alexander Romanovich Luria, both from the USSR. A few of the topics to be considered are the phylogenesis of the brain and, in ontogeny, the biochemical and physiological maturation of neural function. Emphasis will also be placed upon the ontogenetic maturation of behavior and upon the development of speech and language capacities in man.

*Fremont-Smith:* As this conference is sponsored jointly by the National Science Foundation and the Josiah Macy, Jr. Foundation, a few further words on its background might be of interest. When Mr. James M. Mitchell, now Consultant for the National Science Foundation, was its Associate Director, in which post he continued for some time, he and I discussed the possibility of this conference, and it is largely because of his insight and vigor that the National Science Foundation has been able to develop the plan for this series of meetings.

*Mitchell:* For some years I have heard about these conferences but have never had the pleasure of attending one. I am at present involved in another conference program, one with the Brookings Institution. This is a conference series on public affairs, in which problems of public policy in the broad sense are dealt with. So, I might say that I am really here in two capacities: I am representing the Brookings Institution, because we are interested in your techniques of conference management, and I am also representing the National Science Foundation, for reasons stated previously.

As a representative of the National Science Foundation, I might review what this organization has accomplished in the 8 years of its existence. It was originated in 1952 to meet a great national need for some organization that would be devoted primarily to the support of basic research in the sciences in this country. The suggestion for this organization had come from the scientists themselves, in a well formulated statement. Actually, the physical and the biological sciences were the ones that the originators of the Foundation had in mind, although the National Science Foundation now does provide support for a small but growing program in the social sciences.

There are several other current activities of the Foundation that are of importance. One major enterprise is the encouragement of the training of scientific personnel. For this purpose, summer institutes for science teachers and academic year institutes of various kinds are being held. These institutes, we feel, are making a worthwhile contribution.

In addition to supporting basic research, the Foundation provides financial aid to major facilities which are beyond the reach of our universities. For example, the Foundation has supported the establishment and construction of an impressive program in radioastronomy. This is still in the period of organization, but the astronomers feel that it will enable them to make important advances in their field.

Another activity of the Foundation is in the whole area of gathering facts about science. Actually, very little is known about how science has been supported in this country, or who has been engaged in research, not only in this country but in others as well, so the National Science Foundation has undertaken the responsibility of determining these kinds of data.

And lastly, there is the whole area of the support of facilities for the exchange of scientific information, such as translation activities, research and mechanical translation, and publication activities. This, of course, is the reason for the National Science Foundation's interest in the Macy conferences and in this cooperative enterprise.

*Rappleye:* It is a great pleasure, Dr. Fremont-Smith, to join with you in extending a welcome to all the members and guests of this conference. We are particularly delighted with our foreign visitors and hope very much that they will enjoy and benefit from their experience with us, as I know we shall benefit greatly from having them with us. We hope, especially, that they will return to their native countries with a real understanding of the method by which we, in this particular type of conference, are trying to advance knowledge of scientific effort in this country.

We, in the Macy Foundation, look upon the published transactions of the two previous conferences on The Central Nervous System and Behavior as two of the finest books we have issued. Great credit belongs to Dr. Magoun for his chairmanship of the conference, to Dr. Brazier for her editing of the volumes, and to Dr. Fremont-Smith for helping to arrange these activities.

*Fremont-Smith:* As you all know, the spirit of these conferences is quite informal. In line with that, I would like to say that when I find myself being bested in an argument, I often turn to my adversary and I say, "Well, now, would you kindly repeat your basic assumptions?" This nearly always throws him into a state of confusion because he hasn't stated any basic assumptions and, in fact, usually fails to realize that he has not stated any. So I thought I would disarm you right away by giving you my basic assumption, which is that nature is all of one piece; nature does not recognize the artificial separations that the walls of tradition have made between university departments. The branches of science are branches of one science, not separate sciences. Each of these branches has its place; each is as fundamental with respect to the area that it is concerned with as is any other. A study of nature must be a study of nature as a whole. I believe that the multidisciplinary approach is greatly needed, as are scientists who have been intensively trained in two or more disciplines.

I might point out the fact that there is no provision for this at the present time; at least, there is none in our country. In many other countries, there is a less sharp division between the branches of learning than in our own. For example, here, if a man, after having had graduate training in one branch of science, wishes training in another, it is impossible for him to do this without starting all over again, just as though he were a recent graduate.

I think it is quite essential that we give consideration to this need to provide for intensive training in two or more disciplines. This training would not necessarily have to be undertaken serially. I am not at all certain that it could not be done simultaneously, around a problem that requires more than one discipline.

At the present time, there is still a tendency to consider that the only criteria of reliability are those units of measurement in the discipline in which one has been brought up and, to overstate the case, we became milligram worshippers or millimeter worshippers or milliequivalent worshippers or even millisecond worshippers. I would like to emphasize that the scientific aspect of an approach to nature is not determined so much by the precision of the method used, as by the degree of predictability which the approach gives. If an approach gives increased predictability to phenomena, it is scientific, in my judgment. That is my basic criterion of that which is scientific. Precision tends to be worshipped quite regardless of whether or not a high degree of accuracy is necessary for the particular problem on which one is working. As I like to say in this connection, "It is the glory of science to be ever more precise in its methods, and it is the agony of the scientist that when he has been really precise, he finds that what he has measured is just one side of what he is looking at."

The Josiah Macy, Jr. Foundation was started primarily as a grant-in-aid foundation. Dr. Ludwig Kast, the first president, had the strong feeling that foundation executives, as the result of their experience with research projects, grantees, and universities, should be able to contribute something more than funds, that they should be able to share this experience with the people who came to the Foundation either for advice or for funds.

As we examined many projects that came across the desk of the Foundation, we became aware of how unilateral, how single-disciplined, was the approach of most investigators, and also how resistant the majority of scientists was to the idea of a multiprofessional approach. If a pathologist was working on a certain aspect of the liver, and we happened to know that down the corridor from him a biochemist was working on a parallel problem but from the biochemical aspect, we simply could not arouse the interest of the pathologist in the other's work. He would have none of him. But we found that if the biochemist happened to be in another university, perhaps in a distant city, the pathologist was much more interested. So we began to bring together scientists who were of various disciplines and who were from different universities but who were working on a similar problem. This gradually led to the idea of this kind of conference.

I attended many formal scientific meetings in an attempt to learn what really occurred during the sessions, and it seemed to me that the important things took place, not in the meetings, but at odd moments—in the corridors, in the lounge, or at the table. The real communication took place completely outside the meeting rooms. So we decided to try to bring into the conference room some of what usually takes place outside it.

We also thought of our conferences as an exercise in communication. We realized that society has made a great invention for the purposes of communication, but it is very rarely used in scientific meetings. This invention is conversation. I like sometimes to contrast a conversation with a speech. In a speech, such as you are now hearing, the primary purpose of the speaker is not communication. His primary purpose is to hear himself say what he has planned to say. Communication is more or less incidental, if it takes place at all. However, in a conversation, there is a give and take. By a mutually corrective process the two people keep each other on the same wavelength, and as soon as one says something that the other doesn't understand or objects to or gives him an idea which he wants to express, he breaks in. Thus, this mutual feedback system keeps the lines of communication open, or indicates clearly when communication has broken down.

A conversation, as opposed to a speech, we feel, is *par excellence* the method of real communication, of really thrashing a problem out, of being able to ask a question when it comes to mind, rather than losing it because of having to wait until the end of the speech when it may have become irrelevant. It was relevant at that moment when the question arose, and it may not be possible to listen intelligently to the rest of what is being said without having the answer.

Similarly, one's idea, sudden association, or quick memory of something that one hadn't thought of for years needs to be brought into the discussion at the time it comes to mind, rather than be postponed until it is no longer relevant. We therefore try to develop a group conversation at our conferences.

I also like to comment on the fact that in our usual efforts to communicate we tend to give too much attention to our transmitting sets and too little attention to the other fellows' receiving sets. These receiving sets have in them distorting lenses, blind spots, and deaf spots, and it is very important that we give more concern to these factors. This is facilitated if the other person is able to interrupt and express his doubts.

The aim of this particular series of conferences, as Mr. Mitchell has pointed out, is to try to bring before American scientists and scientists from abroad, the great advances that have been taking place in the Soviet Union—advances of which, to a large extent, we have been far too ignorant. It was for this particular purpose that the National Science Foundation asked the Macy Foundation to join them in this series of conferences. We are particularly grateful to the National Science Foundation for providing us with a series of translations of Soviet articles dealing with the general subject matter of each of the conferences.

I would like to speak of one last item; that is, the World Mental Health year. The World Federation for Mental Health is a nongovernmental, international body, with headquarters in London. It is also a multiprofessional body which includes all the disciplines concerned with human behavior. The Federation has established 1960 as the first World Mental Health Year.

# BACKGROUND AND INTERESTS OF THE PARTICIPANTS

**CHAUNCEY D. LEAKE:** I acquired my interest in behavior mechanisms here in Princeton. Forty-five years ago I wrote a thesis comparing the anatomical structure of the brain and skull of the chimpanzee with those of man. I have always been interested in the field, although I went on into physiology and pharmacology at Wisconsin, California, Texas, and Ohio. However, I have always remained curious about the correlative factors that bring us human beings to the behavioral patterns that we show.

**JOHN C. LILLY:** I started out in physics and, after a brief sojourn in biochemistry, went into physiology, in which field I remained for a while.

My present research involves the cetaceans, which have even larger brains than man, although no one knows why. That is what we are trying to find out at the present time.

**KARL H. PRIBRAM:** Among the many things that have interested me are neuroanatomy and neurosurgery, medicine, and primate psychology, to which I came through the study of the human brain. At present, I am testing children in a nursery school, which is a new experience for me and a rather challenging one. Last year at this time, I was interested in computers and computer analogies to brain function, and I am still interested in them.

**ECKHARD H. HESS:** I am a psychologist, with my major interest in problems of perception, particularly on the visual level, and the problems of unlearned behavior. In this latter aspect of my interest, we have been working to a large degree with the very early experiences of animals, studying the phenomenon of imprinting and also trying to follow the maturational changes that occur, in some instances, during the very first hours of the developing organism's life. Most of our work has been with fowl, although we have worked with mammals. In relation to this, we are also attempting to use the technique developed by Erich von Holst in Germany, using brain stimulation, not so much for localizing the places where certain stimulations produce certain results, but as a tool for working out the dynamics of the behavior, largely on a maturational level.

**EUGENE ROBERTS:** I am a biochemist, and I certainly have come into this area by the back door. I have been interested chiefly in the operation of various metabolic systems in different cell types. In 1949, in the course of a still-continuing study of the chemical properties of normal and neoplastic tissues (7), we discovered $\gamma$-aminobutyric acid (GABA) in the brains of vertebrates and found it to be present only in the tissue of the central nervous system. This was tremendously exciting to me, because I felt that a substance with such a unique distribution might have some very characteristic properties which might make it important for the function of the central nervous system, although one eminent biochemist suggested at the time of the first report that GABA might be merely a metabolic waste product. For years we studied the metabolism of GABA in much the way that biochemists study the metabolism of any substance in any tissue. This biochemical area only became of broader interest when the work of biologists and physiologists indicated that GABA might actually play a direct or indirect role in the regulation of neuronal activity. Killam, Purpura, Grundfest, and Jasper among others did pioneering work in mammalian systems, while Wiersma, Florey, Kuffler, Edwards, and others opened the areas in invertebrate physiology.

I was fortunate to be in the Los Angeles area at the time that some of these biological developments were taking place and received great stimulation and encouragement from Dr. Magoun's group at the University of California at Los Angeles and the groups of A. Van Harreveld and C. A. G. Wiersma at the California Institute of Technology. Because of these contacts, I came to hope that a chemist might actually participate meaningfully in studies which could give greater understanding of the function of the nervous system and, possibly, eventually of behavior.

**CHESTER E. LEESE:** I am basically a physiologist. I have just learned with interest that my first psychophysiological contacts with behavior as a student were similar to those of Dr. Kelly, who is with us at this conference. I preceded him by a few years at the State University of Iowa, where we both were behaviorally oriented by several of the same instructors and research personnel. I feel certain that we shall never forget the early experiments of Dr. Travis and Dr. Metfessel, particularly in the area concerned with electroencephalography and the possible influence of brain structures on behavior. These men and others in the department of psychology at Iowa were influential in the lives of many of us who continued in psychology, physiology, and medicine.

**WAGNER H. BRIDGER:** I am a psychiatrist. In addition to formal clinical training, I spent some time with Horsley Gantt at the Pavlovian Laboratories at Johns Hopkins. My work there led me to appreciate the Pavlovian approach to psychic functioning—to consider psychology as a functional product or property of the physiological processes in the central nervous system, but not reduced to those processes. With this in mind, I have always felt that behavioral scientists should try to formulate their theoretical concepts in terms of what is known about the physiology of the nervous system, and that physiologists should try to answer the specific questions that the behavioral phenomena present to them.

As for my own personal work and research, it has evolved toward two basic approaches—one regressive, the other developmental. On the one hand, I have been trying experimentally to alter levels of consciousness in the mature organism in order to break down and analyze the various aspects of cognitive functioning. On the other hand, I have been working in the area of child development which, in a way, can be considered a nodal point of transition from one level of organization to the next—from physiology to psychology, a level at which anthropological and social factors play a crucial role.

**EDGAR L. LOWELL:** I am a psychologist, and my primary interest is in the communication problems of congenitally deaf children and the education of their parents to participate in their training. In the pursuit of this interest, I have been led to a study of brain function, particularly of the auditory system and, currently, I have been led to the application of computer techniques to the evaluation of auditory functioning.

As for my background, I was trained at Harvard in the Department of Social Relations, which involved anthropology, sociology, clinical psychology, and social psychology.

**DOMINICK P. PURPURA:** I am a neurophysiologist with a background in clinical medicine. This conference affords an opportunity to discuss a number of problems which have recently been of particular interest to me. One of these relates to a statement by Ludwig Edinger which is quoted by Herrick in *Brains of Rats and Men*, published some 34 years ago (1). Edinger said, "In order that any particular mechanism may be understood, we have only to discover the species of animal or the favorable developmental stage of an animal in which it is present in so simple form as to be fully intelligible." While this is a guiding principle of general physiology, with respect to the cerebral cortex one wonders whether one can ever hope to find a species or a favorable developmental stage of an animal in which a particular mechanism may be present in so simple a form as to be fully intelligible. I make this statement on the basis of some of our most recent work on the immature mammalian cortex and the cerebral cortex of the reptile. We have found the cerebral cortex of the near-term fetal and newborn cat to be extremely complexly organized, and the turtle cortex has distinctive functional characteristics that introduce a variety of new problems to be analyzed. We can hope to uncover principles of operation of cortical organizations in different species and at various stages of development, but one thing seems certain: Nothing is simple as long as one is analyzing the activity of a neuron which is synaptically influenced by the activity of another.

*Pribram:* The maps that Bailey and Von Bonin made show that the simplest cortex is that of the human being.

*Bodian:* I would like to mention something that was memorable in my experience as Herrick's student. Herrick often told of his incentive in analyzing the amphibian brain in order to study a "simple" vertebrate. He never failed to conclude by expressing his extreme disappointment that it didn't in fact turn out to be simple.

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**HAROLD A. ABRAMSON:** If you want to communicate with an animal, in the type of experiment that I have been doing, the human brain is certainly the simplest of all. I have always been asked why I study drugs like the psychotomimetic drugs, such as LSD-25 or psilocybin, on man rather than on the rat, a lower form. My answer is that man is the simplest animal to work with and possibly, from one point of view, he has the simplest type of brain, that is, if the communication process is to be utilized.

I began in this field many years ago, in chemistry; I then gravitated through medicine, and was influenced by the Macy Foundation and Dr. Fremont-Smith to study the organism as a whole, that is, to bring in the psychodynamic aspects of behavior as well as the model aspects. Through a series of accidents, I became interested in the psychotomimetic drugs, and for the past 10 years have been mapping very carefully, on both nonpsychotic and psychotic subjects the large variety of compounds that has been made available. This group of compounds includes lysergic acid diethylamide and its derivatives, and now 4-hydroxydimethyltryptamine and its derivatives. Using both fish and man as subjects, I have been studying the effect of different chemicals, trying to block the reaction; I have also studied mechanisms of tolerance in both nonpsychotic and psychotic subjects.

**WILLIAM F. WINDLE:** I am primarily interested in the brain stem and spinal cord. However, about 40 years ago I began my work in research with Dr. C. C. Little at Cold Spring Harbor, and at that time we were working on the spleen in mice, doing auto-, homo-, and hetero-transplants.

**GEORGE A. KELLY:** I am now in the Department of Psychology at Ohio State University; however, I started out in mathematics and physics. I then became impatient with the basic assumptions which seemed to underlie these disciplines, so moved into the sociology of education, finishing my formal education thinking that I was going to become a physiopsychologist, but I never did.

I suppose I am a personality theorist as much as anything, and interested in science, though I am not sure that I am a scientist, nor even that I want to become one. It struck me one day that my colleagues and I had been referring to the motivation and the behavior of scientists as based on prediction of events, and that if one wished to understand the march of science through the centuries, one would say it was a march toward better prediction. My colleagues in psychology and I were saying the same thing about psychology as a science, but I noticed, when we started talking about people, we used another set of assumptions. We assumed that ordinary people were not motivated by seeking the future or by making predictions. They were motivated by needs and wishes and impulses. Apparently, we had one set of assumptions for talking about the behavior of man, the scientist, and another set of assumptions for talking about human beings.

It occurred to me that it might be interesting to turn this around and if, instead of looking upon scientists as unusual human beings, we looked upon all human beings, both scientific and nonscientific, as having the same basic motives and the same basic processes going on. Thus, in the sweep of centuries, a personality psychology might be evolved, based upon predictions that the individual man makes. All of this, then, has to do with a psychology of assumptions and an attempt to understand man in terms of his basic assumptions.

**ROBERT A. HINDE:** My training was in zoology, and I did my first research work on birds that were living free in nature. Since then I have been trying to work out, under rather more controlled conditions, some of the problems which were posed by the animals in their natural surroundings.

I am interested especially in the problem of "motivation," and in the influence of learning on the sorts of behavior that were classically called instinctive, though I know Dr. Hess likes to call it "unlearned" instead.

**ALLEN D. KELLER:** I am a mammalian physiologist with special interests in the regulating function of the nervous system and the endocrine system. My interest in the nervous system definitely derives from those with whom I came in contact during my graduate and early postgraduate work. Sutherland Simpson, James W. Papez, and John F. Fulton. In addition, I derived a great stimulus from the literature that I read as a graduate student, in particular, the work of Bechterev in Russia.

**WILLARD C. RAPPLEYE:** I am perhaps an outsider in this particular group because my life has been devoted largely to studying the functions of medicine in modern society; this includes medical education in this country as well as abroad, medical insurance, hospital plans, and activities of that type.

My original inspiration for science and for clinical medicine came from working in the laboratories of Walter Cannon, Otto Folin, and Elmer Southard, and later at the Massachusetts General Hospital. I then went to the University of California, where I worked under Walter Bloor in biochemistry, from which I was diverted into the field of administration.

**ORR E. REYNOLDS:** I think I can trace the history of how I happen to be present at this conference. Dr. Roberts said that he had come in through the back door. I think that I must have come in through the skylight, because my introduction to the nervous system really came through studies in aviation physiology during World War II. My work in aviation physiology turned up a problem involving the nervous system, about which I found I knew little; however, I was very interested, and as a result of my work with simple systems I was invited to one of the Macy Conferences on Nerve Impulse. Later, when I was with the Office of Naval Research, we grew to feel that there was a need for considerably more intensive investigation of the pharmacology of the nervous system, so I brought a request to the Macy Foundation that they sponsor a series of conferences on neuropharmacology, which has been done.

**ROBERT W. DOTY:** One of the reasons for our being here is because 500,000,000 years ago a series of Tunicate-like forms gradually discovered by "genetic experimentation" that they could profitably exchange the certainties of a sessile life for the hazards of moving from place to place throughout their life cycle. This was a profound change in their life pattern. It brought the organism continuously from the known to the unknown, and the organism evolved to cope with the mystery of what lay ahead. Starting with this venturesome biochemical machine, the Tunicate larva, after another five hundred million transformations of its encoded desoxyribonucleic acid sequences, has produced the goal-seeking, statistical guidance mechanism: the human brain, a machine of ten billion units with enough excess circuitry to analyze the unknown of itself! After my service in the Army during the war, my own ten billion neurons came under the influence of Dr. Ralph Gerard's eleven billion, and it was then inevitable that I should become a neurophysiologist.

**ERIK H. ERIKSON:** I am a psychoanalyst and am affiliated with the Austin Riggs Center. This is a residential center for treatment and research in severe neuroses, and for patients on the borderline of neurosis and psychosis. The senior staff consists entirely of psychoanalysts, but we are very much interested in those matters which have not been investigated as yet in psychoanalysis—matters of will, and, especially, of work and the role that these factors play in a patient's motivation for *getting* well, at the same time that the dynamic reasons for his not *being* well are being elucidated. I am therefore particularly interested in being here and in learning about any studies that are being carried out on language. I am not a physician, and for that reason, more than any of the rest of you, I am here as a student.

I might mention, to establish a common bond with some of the other participants, that I am about to leave clinical work as a main occupation and go into teaching at Harvard. So, while I doubt that I can contribute anything to your deliberations, I can promise that I am going to transmit whatever I shall learn (or unlearn) to young people who in the future may contribute to your work.

**EUGENE NIKOLAIEVICH SOKOLOV:** I am affiliated with Moscow University, and my main interest is the application of reflex theory to the problem of perception. This interest was first aroused during my work in Professor Kravkov's laboratory. This laboratory was established after the Great October Revolution and has focused on the problem of perception, with especial interest in sensory interaction.

Since 1950, in my research work, I have been trying to integrate the data and theory of higher nervous activity with achievements of electrophysiology by applying precise measurements used in the psychophysiology of sense organs. The results of the experiments in the laboratory are applied to the study of impaired sense organs in children, in the Institute of Defectology of the Academy of Pedagogical Sciences, USSR.

I am happy to attend this conference, which is a multidisciplinary discussion like the "Wednesday meetings" Pavlov used to hold in his laboratory, at which problems of higher nervous activity were discussed, the participants being psychologists, psychiatrists, physicians, and mathematicians.

**ALEXANDER ROMANOVICH LURIA:** I am a psychologist, and I come from the Soviet Union. I was graduated twice: The first time was in 1921 as a psychologist from the Department of Social Sciences of the University of Kazan, one of the oldest universities in our country, and the second time was from Moscow Medical School. I attended the latter because I felt that I needed the double background of psychology and of neurology.

From the first days of my scientific work, I was deeply influenced by the two-fold tradition of Soviet science, which has a close connection with the philosophy of dialectical materialism. There is, first, a tradition of objective approach to behavior and to the study of the mechanisms that underlie behavior. It was Sechenov who originated this approach, and the generation of psychologists to which I belong was deeply influenced by it. But I was also deeply impressed and influenced by another part of this tradition, which was the *developmental approach* to all problems and especially to the problems of psychology and physiology. That is why I wanted to combine both the objective approach to the mechanisms and the developmental approach to the process of formation of the highest levels of behavior.

While I was in my twenties, I began to work on the application of objective study to the organization and disorganization of human behavior. My book (6), which was translated into English by Dr. Horsley Gantt and published nearly 30 years ago, was devoted to the problem of the mechanisms of organization and disorganization of behavior.

While I was working in this field as a young man, I met Professor Leo Vigotsky, the most distinguished psychologist in our country; we became great friends, and this meeting played a decisive role in my own development. From then on, I became extremely interested in the mechanisms of the development of the higher forms of mental functions. I undertook a series of psychological experiments with Professor Vigotsky, analyzing how these highest mental functions came to develop, and carried them on many years after his death. I spent several years in analysis of the development of higher nervous activity in normal and abnormal children, and I shall report some data from these studies in our conference.

These interests led me to the analysis of local injuries of the brain and to the problems one meets in the psychological service of the neurosurgical clinic, including both diagnosis and rehabilitation.

That has been my interest in the last two decades. I study the analysis of the local injuries of the brain, the psychological approach to them, and combine these with a physiological analysis of the mechanisms underlying the disturbance of the rehabilitation functions. I am very indebted to Dr. Fremont-Smith and to Dr. Magoun for inviting Professor Sokolov and me to this conference.

**FRANK FREMONT-SMITH:** When I was a student at the Harvard Medical School, I became fascinated with a clear, limpid fluid, the cerebrospinal fluid, and, after my internships in pathology and medicine, I was invited by Dr. James B. Ayer to study this fluid in his laboratory at the Massachusetts General Hospital. I remember the rather remarkable introduction that I had to this research. Dr. Ayer took me to the laboratory and then he started to leave. I said, "But, Dr. Ayer, what shall I do?" Over his shoulder he said, "Do some research," and left me, which was, I think, a very nice way to start a person off in the field.

One of the things I tried to measure with precision was the pressure of the cerebrospinal fluid, because many of the patients with whom I was working had convulsions and showed signs that seemed to indicate possible brain tumor. Then, I discovered, to my surprise, that it was not easy to measure the fluid pressure even though the patient lay with his spinal column in a horizontal position, because if he was under tension and tended to hold his breath, his venous pressure would rise, and then his cerebrospinal fluid pressure would rise, and one might suspect a brain tumor when none was present. If, on the other hand, the patient, being rather tense, began to overventilate, as some patients do, the venous pressure would go down, the cerebrospinal fluid pressure would go down, and a normal pressure might be measured when it was really elevated. This led me into the field of the influence of emotional factors upon the physiology of the organism, the area now known as psychosomatic medicine. In this manner, I gradually entered the field of psychiatry, by the back door, one might say.

Then I must tell you how I gained my reputation as a psychiatrist. It was all the result of my first consultation with a patient. At this particular time, I had been moving about in my work from the cerebrospinal fluid to other body fluids, amniotic fluid and joint fluid, and so forth. I became very interested in tears, but, because of the rather primitive methods that were in use in those days, I could not collect enough tears for measuring salt content. I was just about ready to give up this important research when I had this first psychiatric consultation. The patient was a nurse, and she had been weeping for 48 hours and could not stop. No one knew what to do, so I was asked to see her. I took with me two clean test tubes, thinking that at last I was going to be able to collect enough tears for my project. The patient was sitting up with tears streaming down her face. All these beautiful tears, I thought, going to waste. I said, "We're extremely sorry about your problem and we are certainly going to help in every way we possibly can, but it's going to take just a little while to do it, and, in the meanwhile, I wonder if you would be willing to help us?" I explained to her our problem and how desperately we needed some tears. I brought out my two test tubes, and I said, "Would you be willing to hold one on either side of your nose for the next twenty minutes?" She took one look at me and one look at the test tubes and stopped crying. Of course, I was in despair, but I made my reputation as a psychiatrist.

My subsequent history, you all know. I came to the Foundation in 1936 and have been very happy, bringing my friends or soon-to-be friends to conferences. It has been a great privilege to have this opportunity.

**H. W. MAGOUN:** I would like, if I may, to recall an August Saturday in Chicago, many years ago, when a group of young graduate students escaped from the city heat and the confines of the laboratory and their studies, to the Indiana dune country on the southern shore of Lake Michigan. The rolling palisades of yellow sand, coming up from the blue lake, with scrub pine and oak at the top, made an ideal vacation setting. About noon, however, an Indiana summer thunder storm came up, and there was a deluge.

To protect the basket lunch, we approached a frame cottage at the top of the dune, to ask if we could put it under shelter. A canvas was stretched out from the side of the cottage and under it, in a deck chair, was a rather slight, tanned, clean-cut man in a pair of pajama bottoms. Near him were two or three volumes of philosophy which he had been reading. Putting his books aside, and with the most gracious cordiality and friendliness, he invited us to join him for lunch.

As we lunched, sheltered from the rain, he began to tell us about his scientific life and how he had been motivated to begin a study of the comparative anatomy of the nervous system, although he emphasized that it was undertaken as a basis for understanding the maturation of function and behavior rather than from a strictly morphologic interest. He told us also how, through the loss of his brother, who had died very early in his career, he had derived an incentive to continue to carry out his brother's plans and goals.

He went on to the associations that he had enjoyed with Coghill, who had similarly made efforts to investigate the maturation of behavior in lower vertebrates, and he described camping trips they had taken in the Grand Canyon area of the West. He explained how his interest had become increasingly aroused by the philosophical aspects of his study of the brain and behavior.

I do not believe that any group of graduate students ever enjoyed a visit more than this group, who had just by chance sought shelter from a thunderstorm and been entertained in this wonderful fashion. As you may have guessed, this was C. J. Herrick, who used to take refuge from Chicago every summer by repairing to his little cottage among the Indiana dunes.

It seemed appropriate at this time to recall that occasion, because just a few weeks ago Dr. Herrick passed away at the age of 91.

*Leake:* Actually, C. Judson Herrick derived a great deal of his strength and influence, I think, from what he called, at the time, seminars, but they were conferences quite like this. He and his brother inaugurated those seminars at Denison University, which is on a lovely hill in the center of Ohio.

One of the delightful little essays of C. J. Herrick was entitled, "Little Academies That I Have Known." This dealt with similar meetings that had been held in various parts of the country. I think it is also appropriate to recall that his most recent book, which was on the development of human nature, was published only 4 years ago (*The Evolution of Human Nature*) (2).

**JAMES M. MITCHELL:** I was trained as a personnel psychologist and went into the field of public administration, where I have been working for about 25 years, trying to apply what we know about psychology to the problems of public administration. I have done this in the Civil Service Commission, the Department of Defense, and the United Nations, and, for the last 5 years, with the National Science Foundation. Since last July, however, I have been with the Brookings Institution, where we hope to use what we know about methods of communication through conferences with the makers of public policy. When I say "the makers of public policy," I refer to people in the Congress as well as in the Executive Branch.

The Brookings Institution has done research in economics and political science for a number of years, but only recently have we made a positive effort to communicate, not only Brookings research but other social science research, to public policymakers.

*Leake:* I would like to state that the American Association for the Advancement of Science is very grateful for the cooperation of the Brookings Institution in setting up the first seminars of this type.

*Mitchell:* I'm glad you mentioned that, Dr. Leake. As you know, the Executive Secretary of the American Association for the Advancement of Science and I have recently talked about a series of seminars for members of Congress on the frontiers of science, and we have just about concluded an agreement.

**MARK G. FIELD:** Like Dr. Lowell and Dr. Olds, I am also a product of this hybrid Department of Social Relations at Harvard, though my training was in sociology rather than in psychology and cultural anthropology. While at Harvard, through the influence of Professor Talcott Parsons, I became interested in the sociology of the professions, and more particularly the medical profession. Professor Parsons had done a considerable amount of pioneering work on the study of the American medical profession and an affiliation with the Russian Research Center at Harvard permitted me to make a study of the Russian medical profession. My interest is now in comparative medical institutions, particularly on how large-scale industrial systems go about meeting the problems of medical care and public health, including research, financing of training, distribution of personnel, etc.

Recently, I have also become quite interested in what we sociologists call the "process of socialization," which is perhaps another aspect, in the sociological context this time, of many of the problems we are interested in here. By this, I mean a study of the development of the child as shaped by social and cultural processes to enable him, as an adult later on, to fit in the society. How does a society go about changing or transforming the "raw material" that the baby is at birth into an adequately performing member of society. Indeed, the stability and functioning of society depends to a great extent on this process particularly in view of the fact that a social system renews its personnel completely every three or four generations.

In closing, I would like to make an announcement that might be of interest to those of you who can read Russian. I recently received a communication from *Contemporary Psychology*, which is a journal of reviews in the field of psychology. As there is growing interest in the contributions of our Russian colleagues, the consultant on Slavic books (Dr. Joseph Brozek, Lehigh University, Bethlehem, Pennsylvania) is looking for individuals who can read Russian and who could write reviews of psychological and allied work in the social sciences for dissemination to an English-speaking audience. This is a very worth-while project, and I would encourage those of you who read Russian either to contact me or to write directly to Dr. Brozek for more details.

*Luria:* We in Moscow are preparing a series of reviews of contemporary work of social psychologists for the journal, *Contemporary Psychology*, and soon the journal will have my review of Dr. A. N. Leontiev's (5) book on problems of development, Dr. A. V. Zaporozhets' (8) review of my two volumes, a review of a very interesting new book, *The Mechanisms of Speech*, by N. I. Zhinkin (9), and a few other books. That will be our contribution to the friendship among Russian and American psychologists, which we regard as one of our very, very important duties.

*Field:* I appreciate very much this work, and my only purpose in making that announcement was to attempt to lighten your load by enlisting the interest of American psychologists and social scientists in the work being done in your country.

**MARY A. B. BRAZIER:** I am a neurophysiologist, and I work at the Massachusetts General Hospital. My own work has been focused particularly on the electrical activity of the brain. As I listened to the many aspects of brain research that have been mentioned around this table, I noticed that several people have stressed the complexities of their field, but we who work on the electrical activity of the brain perhaps can claim the least understood field of all. Although this phenomenon has now been known for 85 years, we really understand it very little. I come to these conferences with a strong feeling of anticipation that perhaps this multidisciplinary type of discussion may open up a line of thought that could be productive in helping to clear the obscurity that surrounds this field; so I always come with very great pleasure to these conferences.

**DAVID BODIAN:** I have been impressed, throughout this discussion, with the geographical aspect of the study of nervous system in behavior. Although I am in charge of the Department of Anatomy at Johns Hopkins, it was in Chicago that my scientific interest in the nervous system was aroused. I came upon the nervous system through, not a disciplinary window, but an operational window, the microscope.

Although, since then, I have been in and out of direct contact with problems of the nervous system, I have always achieved a great esthetic satisfaction from the microscopic approach. I think that someone should mention that whatever approach we take to the nervous system, there is usually behind it a considerable satisfaction for us in the way we go about it.

**ROBERT B. LIVINGSTON:** The American Physiological Society decided this autumn that they should devote a half day of their annual meeting to a Symposium on the Neurophysiology of Learning and Motivation. Dr. Galambos had the inspiration to invite Professor C. Judson Herrick to be Honorary Chairman of this meeting. In October we wrote to Professor Herrick and received a warm response from him acknowledging his gratitude for this honor "because in the twilight of one's day such expressions of regard by his colleagues are the highest rewards of scientific endeavor." He wrote that he would be delighted to be the Chairman provided that he could be so *in absentia*, because he was not strong enough to travel. Professor Herrick also accepted our invitation to contribute a paper which might be read for him at the meeting. A few days thereafter came a full and interesting paper, composed on his own typewriter and having corrections in his own hand. This represents, as it turned out, the last scientific paper written by Professor Herrick. Following this came several letters from him urging that the participants in the Symposium exchange all of their manuscripts prior to the meeting; in this way each could contribute criticisms and suggestions that would be helpful to the others and thereby assist in the achievement of a better integration and conceptual exchange at the meeting itself.

Shortly thereafter we were all made dreadfully heavyhearted when we read in the newspapers that Dr. Herrick had died on January 29, 1960. A few men should be spared mortality; even though Professor Herrick lived to be 91, we were most regretful that he could not have lived on indefinitely.

Professor Herrick's recent book, *The Evolution of Human Nature* (2), is an inspiring work. He points out that evolution, as it is commonly conceived, places too great an emphasis on conflict as providing the sole or predominant mechanism of evolutionary progress. Biological mechanisms could not have proceeded very far in the evolution of complex forms of life without having first established the underpinnings for cooperation, faith, and mutual trust—beginning with primitive and going on to progressively more elaborate and potentially nobler systems of behavior. The emphasis on conflict alone reveals only part of nature—only part of the vital biological potentialities for liberating and enriching life. Conflict cannot be dismissed, but conflict taken as a lone instrument for evolution is like the odd half of a pair of scissors.

I should like to quote a passage from Professor Herrick's book: "Man's capacity for intelligently directed self-development confers upon him the ability to determine the pattern of his culture and so to shape the course of human evolution in directions of his own choice. This ability, which no other animals have, is man's most distinctive characteristic, and it is perhaps the most significant fact known to science." (2)

*Leake:* In connection with Dr. Herrick's background, I would like to contribute a statement which he formulated with Edwin Grant Conklin, who was Professor of Biology at Princeton. This was made in 1939, in the Santa Cruz redwoods, during a summer meeting of the American Association for the Advancement of Science at Stanford. Herrick and Conklin were debating the background for an ethical basis for science. The point was, would it be possible to formulate a statement of a scientific nature that would have moral significance. They formulated such a statement, which I think is pertinent in any discussion of human behavior: "The probability of survival of a relationship between individuals or between groups of people increases to the extent to which the relationship is mutually satisfying." (3,4). I have never seen that statement challenged.

*Fremont-Smith:* We have been talking about the physiology of the brain, behavior of the brain, as if man behaved by himself. When man behaves by himself, it is a form of abstraction, over and beyond the natural relationships which always exist between individuals. Therefore, I think that we should study and discuss the physiology of interpersonal relationships, which are just as much physiological as psychological.

In reference to the discussion of a scientific statement of ethics, I have wondered for a long time whether, with respect to the conflicts among societies, there was any common denominator to which all peoples in the world could agree. I thought first of religion, but this, obviously, is a source of conflict rather than of communal relationships; then, I thought of culture, and realized that cultural differences are separative rather than unifying; next I thought of biology: What is the most humanly significant biological denominator common to all human beings and to all human groups? It occurred to me that this might be the concern of parents for their very young. This parental concern has a long biological heritage and is absolutely essential for survival of most species. Moreover, parental concern for their very young lies at the heart of the family. And so, it seemed to me that this might also provide an ethical basis, a scientific or biological—I would rather say a biological-ethical basis—of behavior, and that this cooperative necessity between human beings starts with the parent-baby relationship. It is still a dominant need in the world today.

From this, I want to make reference to one other point of view, that of the World Federation for Mental Health and its concern with World Mental Health Year. I have brought out, on a number of occasions, the fact that we now live in a period of history when no nation any longer is strong enough to protect its own children or to guarantee their survival; that the only hope of being able to guarantee the survival of our children, or our children's children, would be for the nations to join hands and protect each other's children. If we could evoke this common concern for the very young the world over, we would begin to develop a very strong motivation toward this mutual protection, which is the only protection that we can hope will work.

I do believe, and this is the position of the World Federation for Mental Health and the basic concept of World Mental Health Year in its long-range thinking, that the branches of science that include the study of human behavior have a contribution to make to the understanding and eventually to the resolution of human conflict. Here, then, is a possibility of building bridges of trust in an area which endangers no one and about which, I believe, every nation could agree. The protection of our children and our children's children is obviously of paramount importance for the future of all. If this could be the basis for a bridge of mutual trust, it could eventually be extended to a concern, not only for children, but for adolescents and even for adults.

## REFERENCES

1. Herrick, C. J.: A survey of the origin and biological significance of the cerebral cortex. *Brains of Rats and Men.* Chicago, Univ. of Chicago Press, 1926.
2. ———: *The Evolution of Human Nature.* Austin, Univ. of Texas Press, 1956.
3. Leake, C. D.: Ethicogenesis. *Scient. Month.* **60**, *245-253 (1945).*
4. Leake, C. D., and Romanell, P.: *Can We Agree? A Scientist and a Philosopher Argue About Ethics.* Austin, Univ. of Texas Press, 1950.
5. Leontiev, A. N.: *Problems of Mental Development.* Moscow, Academy of Pedagogical Sciences Press, 1959.
6. Luria, A. R.: *The Nature of Human Conflicts.* New York, Liveright, 1932. (Translated from the Russian by W. Horsley Gantt.)
7. Roberts, E., and Simonsen, D. G.: Free amino acids and related substances in normal and neoplastic tissues. In: *Amino Acids, Proteins and Cancer Biochemistry.* J. T. Edsall, Ed. New York, Academic Press, 1960 (pp. 121-145).
8. Zaporozhets, A. V.: *Development of Voluntary Movements.* Moscow, Academy of Pedagogical Sciences Press, 1960.
9. Zhinkin, N. I.: *The Mechanisms of Speech.* Moscow, Academy of Pedagogical Sciences Press, 1959.

# THE EVOLUTION OF MAN'S BRAIN

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BEFORE THE NINETEENTH CENTURY, the *Scala natura*, in which living forms were arranged in an order of increasing complexity, was generally conceived as the immutable product of divine creation. Early in the century, Lyell's ideas of geological evolution provided a background for Darwin's proposal of the *Origin of Species by Means of Natural Selection*, published in 1859. By this principle, Darwin wrote, "Light will be thrown on the origin of man and his history," a prophecy fulfilled in 1871 in his *Descent of Man*. Darwin's concept of man's evolution from primate ancestors anticipated the discovery of intermediate fossil forms. In the creationists' view, fossils of lower plants and animals were the consequence of periodic geological catastrophes that had wiped out all life, after which new and higher forms were created. Because, as Cuvier had pointed out earlier, man's creation had followed the last such catastrophe, "L'homme fossile n'existe pas!"

The accumulation of actual evidence for fossil man began with the discovery of Neanderthal remains in 1856. Next, Java man was found in 1891. The implications of both findings were vigorously opposed, the first on the ground that it was a pathological specimen of modern man and the second on the basis that it was a fossil ape. Throughout this period, Darwin's "bulldog," Huxley, defended the concept of man's evolution against the opposition of Richard Owen in England, while Ernst Haeckel played a similar role against Virchow in Germany. In the present century, increasing discoveries of fossil material now make possible the presentations of a well documented series of stages in hominid evolution.

## GENERAL FEATURES OF HOMINID EVOLUTION

Earlier concepts of the evolution of man, in which growth of the brain was considered to be the primary and determining event, have now given way to the view that man's large brain is the culmination of a series of changes which actually began caudally and only reached the cranium through successive alterations in intervening parts of the body.

It is now generally held that the initial adaptation leading to the emergence of the *Hominidae* involved the pelvis and lower extremity, permitting assumption of an upright posture. Following this, the upper extremity and hand, freed from locomotory obligations, undertook the activities of prehension and food-getting, as well as those of combat and defense, for which the jaw and teeth had previously provided the major instrumentation. The acquisition of manual skills, augmented by the use of specialized implements and weapons capable of being sequentially employed and discarded, reduced the requirements for a large jaw with its built-in incisor teeth for cutting, its large canines for attack, and its molars for grinding food. Consequent reduction of the lower face and regression of the massive jaw musculature, which had "imprisoned the cranium," was followed by an expansion of the brain-bearing portion of the head and an hypertrophy of its neural contents.

From the viewpoint of geological time, the interval over which these alterations of hominid evolution proceeded has been described as "explosively" brief. Life is presumed to have originated on this earth some 2 billion years ago, the simplest primates made their appearance 60 million years ago, and remains of fossil apes (*Proconsul*) are dated at 25 million years. By contrast, the entire scope of hominid evolution has occurred within the most recent geological period, the Pleistocene, which spans only the last one million years. Hominid evolution has occupied, therefore, about 0.05 per cent of the total period of life on earth. It is customary to divide the Pleistocene into three subperiods: the Lower (500,000 years), in which the Australopithecines were the typical hominids; the Middle (350,000 years), of which the Pithecanthropoids were representative; and the Upper (150,000 years), characterized by Neanderthal types living 50,000 to 100,000 years ago, and by *Homo sapiens*, present only for the last 25,000 to 50,000 years. The span of existence of modern man is thus only about 0.00125 per cent of the total period of life on earth.

The following general survey of the subject is organized both chronologically and in relation to these stages of hominid development. It is obviously introductory, and technical analysis of proposed taxonomic relations has been studiously avoided.

## AUSTRALOPITHECINES

During 1924, at the Northern Lime Company, Taung, South Africa, there was blasted out of the red, sandy limestone a small fossil brain-cast and skull. The specimen was studied by Professor Raymond A. Dart, of the Department of Anatomy, Witwatersrand University in Johannesburg and, because of its seemingly obvious significance, he promptly sent off to England a preliminary account which appeared in *Nature* in 1925.

"It represents," Dart wrote, "a creature well advanced beyond modern anthropoids in just those characters, facial and cerebral, which are to be anticipated in an extinct link between man and his simian ancestor. I proposed that a new family of man-apes be created, and that the first known species be designated *Australopithecus africanus*, vindicating Darwin's claim that this continent would prove to be the cradle of mankind." The editor of *Nature* requested the leading English anthropologists to comment, and the 5 year-old hominid—"Dart's baby" as the immature Taung skull soon came to be called—was generally condemned as a fossil ape.

In 1936, Dr. Robert Broom of the Transvaal Museum started collecting in the nearby limestone caves and, in two years' time, accumulated several skulls of adult man-apes. Most recently (1959), Dr. and Mrs. L. S. B. Leakey of the Coryndon Museum, Nairobi, discovered in Tanganyika the skull of a type with massive molar teeth, nicknamed "nutcracker man." As Dr. Broom stated: "We now know with moderate certainty that a group of higher primates lived in South Africa in Pliocene time and apparently survived into the Pleistocene. They were almost certainly bipedal and probably used their hands for the manipulation of implements. Their faces were rather larger than those of modern man, but their brains were relatively small. The group, if not quite worthy of being called men, were nearly men."

The Australopithecines now emerge as the main hominid type of the Lower Pleistocene period. Their cranial capacity averaged 550 cc. (450 to 650 cc.), which is but 100 cc. larger than that of the average anthropoid (450 cc.). These small-brained bipeds made crude and simple pebble tools, which have been found with their remains.

## PITHECANTHROPOIDS

The nineteenth-century proposal, by Ernst Haeckel, that man had evolved from a gibbon-like ancestor in Indonesia led young Eugene Dubois, physician in the Royal Dutch Army, to seek assignment in Java to undertake excavations exploring Haeckel's view. In 1890, Dubois discovered a calvarium, femur, and jaw in a mid-Pleistocene stratum, on the bank of the Solo River in Trinil. These findings were described in a monograph entitled *Pithecanthropus erectus; eine menschenaehnliche Ubergangsform aus Java*, published in Batavia in 1894. Later, exhibit of his specimens in Europe was met by so much opposition that Dubois withdrew the material and locked it away from examinations for most of the rest of his long life. His confidence was not shaken, however, and he later wrote: "I believe that it now hardly admits of a doubt that this upright-walking ape-man, as I have called him, represents a so-called transition-form between men and apes. I do not hesitate now, any more than I formerly did, to regard this *Pithecanthropus erectus* as the immediate progenitor of the human race."

Confirmation of his conclusions came in 1927, when Davidson Black, Professor of Anatomy at Peking Union Medical School, China, boldly published a paper on a fossil hominid molar tooth, excavated from the quarries of Chou-kou-tien, southwest of Peking. "The circumstances," Black wrote, "justify the proposal that the hominid be regarded as a new genus to be named *Sinanthropus*. Since the horizon from which the specimen was obtained is identical with the early Pleistocene, the hominids of Chou-kou-tien occurred contemporaneously with *Pithecanthropus*." In extensive succeeding excavations, remains of upwards of forty individuals were discovered and, following Black's death, their study was continued by Franz Weidenreich. Upon the Japanese invasion of China, U. S. Marines attempted to evacuate the collection to the Chinese coast for transport to this country but they were captured by Japanese troops. The subsequent fate of the collection has remained to this day a mystery. Meanwhile, further exploration in Java, by G. H. R. von Koenigswald, revealed additional remains of *Pithecanthropus* which he studied with Weidenreich following World War II.

Java and Peking man are now considered members of a common Pithecanthropoid group forming the dominant hominid type of the middle Pleistocene period. The cranial capacity of Java man averaged 850 cc. (750 to 900 cc.) and that of Peking man 1,050 cc. (900 to 1,200 cc.). The latter made chopper-type tools and weapons, somewhat more elaborate than those of the Australopithecines, but crude by comparison with the later cultures. Peking man was a hunter and, above all, was distinguished by introducing the use of fire.

## NEANDERTHAL MAN

Neanderthal man gained this appellation from the discovery of his remains in a cave in the Neander Gorge, near Dusseldorf, Germany, in 1856. Neanderthaloid remains, since discovered widely in other parts of Europe, and in Africa and Asia, may be considered representative of the main hominid type of the Upper Pleistocene period. His cranial capacity averaged 1,350 cc. (1,150 to 1,600 cc.), a figure within the limits of modern man. The pointed flints and hand-axes of Neanderthal man were improvements over earlier tools and weapons. Caches of bear skulls in his caves suggest the possibility of ritualistic activities. Recovery of the remains of the old man of La Chapelle aux Saints from a shallow grave provided the earliest instance of man's burial.

Limitations of his cultural advance, despite an essentially modern cranial capacity, have probably been responsible for the lowly status in which Neanderthal man was formerly held. M. Boule, who reconstructed the skeleton from La Chapelle aux Saints in a semierect, simian-like posture, wrote: "The uniformity, simplicity and rudeness of his stone implements and the probable absence of all traces of preoccupation of an aesthetic or moral kind, are quite in agreement with the brutish appearance of this energetic and clumsy body and heavy-jawed skull, which itself declares the predominance of functions of a purely vegetative or bestial kind over the functions of the mind."

Recent celebrations of the centenary of the discovery of Neanderthal man have tended to elevate his position somewhat. Straus and Cave concluded: "There is no valid reason for the assumption that the posture of Neanderthal man differed significantly from that of present-day man." Eiseley wrote: "Let us remember what was finally revealed at the little French cave near La Chapelle aux Saints. Here, across millennia of time, we can observe a very moving spectacle. Massive, flint-hardened hands had shaped a sepulchre and placed flat stones to guard the dead man's head. A haunch of meat had been left to aid the dead man's journey. Worked flints, a little treasure of the human dawn, had been poured lovingly into the grave. For these men whose brains were locked in a skull reminiscent of the ape, these men whom serious scientists had contended to possess no thoughts beyond those of the brute, had laid down their dead in grief."

## FOSSIL MODERN MAN

Just as the discoveries of the Australopithecines had a particular setting in Africa, and those of the Pithecanthropoids in Asia, so the crowning stage of hominid evolution, fossil *Homo sapiens*, was earliest found and most thoroughly investigated in Europe. Southern France especially provided large collections of the remains of Ice Age, Stone Age, or Reindeer Age man, as he is variously called.

During the 1860's the French anthropologist, Édouard Lartet, and his patron and collaborator, the English industrialist, Henry Christy, recovered quantities of Ice Age artifacts from the Vézère Valley in Dordogne, France. This "paradise of primitive man" came to have a meaning for prehistory, like that of the Valley of the Kings in Egyptology. In 1864, Lartet's work was crowned by finding a mammoth's tusk, upon which the picture of a mammoth had been engraved, an overwhelming proof that primitive man had lived early enough to have known the mammoth. In 1868, during railway construction, the Cro-Magnon cave was discovered. In it, Lartet's son, Louis, found remains of weapons, tools, ornaments, game, and five human skeletons, including "the old man of Cro-Magnon." His striking skull, with high forehead, broad face, and prominent nose and chin, became the type-specimen of Cro-Magnon man, the earliest representative of *Homo sapiens*, living 50,000 to 25,000 years ago.

The skeletal remains of the Cro-Magnon cave were studied by the anthropologist, Paul Broca (1824-1880), better known today for his discovery of the cortical speech area. Broca's presentation to the French Society of Anthropology, in 1868, opened: "The innumerable objects found in the caves have not only furnished the most incontestable proof for the contemporaneity of man to mammoth, but here revealed also the most curious details of the life and manners of these ancient troglodytes. There still remained to be known, however, the anatomical characteristics of this intelligent and artistic race, whose carvings are a subject of astonishment for us. This lacuna has been filled in today by the bones presented by M. Lartet fils."

Endocranial casts of Cro-Magnon man, taken from the Predmost skulls from Moravia, had cranial capacities ranging from 1,308 to 1,568 cc. and averaging 1,435 cc. The capacities of other specimens are 1,415 cc. (Combe-Capelle), 1,590 cc. (Cro-Magnon) and 1,530 cc. (Chancelade). An over-all average of 1,475 cc. is sometimes given, equivalent to or slightly larger than that of contemporary man (1,450 cc.).

While physical anthropological interest in fossil *Homo sapiens* has recently come to lie chiefly in technical questions of racial relationships, the cultural features of his development have been of the greatest general interest. In the long series of stone artifacts marking hominid evolution, crude and stereotyped tools and weapons of earlier manufacture can readily be distinguished from the later ones of *Homo sapiens* with their contrasting inventiveness, variety, and perfection. S. L. Washburn has stressed the important role played by tools in hominid evolution. "It is my belief," he writes, "that the decrease in the size of the anterior teeth and the tripling of the size of the brain came after man was a tool user, and were the result of new selection pressures coming in with the use of tools." Later he summarizes, "It was bipedalness which started man on his separate career. But tool use was nearly as early. Biological changes in the hand, brain, and face followed the use of tools, and were due to the new selection pressures which tools created. Tools changed the whole pattern of life—bringing in hunting, cooperation, and the necessity for communication and language. Memory, foresight, and originality were favored as never before, and the complex social system made possible by tools could only be realized by domesticated individuals. In a very real sense, tools created *Homo sapiens.*"

While some of the implements of the Cro-Magnon period came to be decorated by their makers, artistic interests were by no means confined to this utilitarian association. Animal carvings on bone, prepared by Cro-Magnon man, attracted earliest attention, but his paintings, discovered later on the cave walls of Southern France and Northern Spain, formed his greatest cultural achievement. The art of Reindeer man, the hunter, was dominated by the major source of his food supply, before which he was extremely self-effacing. Vegetable forms are exceedingly rare; some fish and birds are represented, but the large mammals, which he hunted, are figured in prolific variety and abundance.

Most frequently depicted are the reindeer, cave bear, bison, rhinoceros and, most impressive of all, the now extinct mammoth. The creative artistry of these paintings suggests that they formed expressions of man's early esthetic interests. Additionally, it is likely that these animals were drawn upon the cave walls and missiles directed at them in rites promoting success in hunting, designed to insure the food supply and material welfare of the practitioners. Man did not dwell in these caves that he decorated, but seemed rather to have entered their dark interiors for magical or sacred rituals. These subterranean caverns appear to have formed early religious sanctuaries for Ice Age man. A striking instance, in the cave of Trois Frères, is "The Sorcerer" who presides over a chamber filled with paintings of animals of the hunt. He has the horns of a stag, the face of an owl, the ears of a wolf, the forelegs of a bear, and the tail of a horse. His arms are flexed and his feet appear to move as in a dance; his virile reproductive organ is paradoxically pointed backward. The archeologist, Abbé Breuil, concludes, "Such is the figure the Magdalenians considered the most important in the cave and which we judge to represent the spirit ruling over the abundance of game and the hunt's success."

The Venus of Willendorf is one of the "steatopygous aphrodites, with their voluminous breasts, prominent hips, and protruding buttocks," which seemingly characterized the feminine ideal of Ice Age man. Discovered in 1908 by a road builder in the village of Willendorf, Austria, it is attributed to the Aurignacian Period. The archeologist Hugo Obermaier remarked: "Its maker had a first-rate comprehension of the build of a human body, but was only concerned in this case with bringing out the primary and secondary sexual characteristics." A desire for increase and fertility has been proposed to account for the abundance of these forms, which emphasized prolific femininity to the point of deformation.

A number of the caves contain paintings of the hands of prehistoric man. Most of these are imprints, silhouettes, or stencils: one hand was held against the cave wall and surrounded by pigment applied with the other. The left hand is usually shown and, in one cave, thirty-five left and seven rights hands were so depicted. The right hand of Ice Age man was thus more frequently employed for dextrous manipulative activity than his left. Such right-handedness is associated with left cerebral dominance and, in turn, is related to the representation of the cortical mechanism for speech in modern man. Though man's first records of written language do not appear until about 5000 B.C., frequent dots, lines, and geometric patterns in many of the caves suggest the beginning use of symbols at this much earlier period.

Most fascinating of all is the possibility that primitive man may already have developed concepts of possession of a soul and its leaving the body after death. The dramatic scene of the "Man in the Well" at Lascaux shows a rhinoceros and a disemboweled, but still standing bison, with a spear through its flank. Between them, a man lies prone and outstretched, his face masked as a bird. Obviously the man had speared the bison, possibly after it had been gored by the rhinoceros. One or the other of these beasts must then have killed the man. His conspicuous priapism may have been the consequence of injury to the spinal cord, or of autonomic discharge associated with death in struggle. Most interesting of all is a small bird perched, like a weathercock, on a rod in the foreground of the painting. Does this represent the dead man's soul?

## THE BRAIN OF MODERN MAN

The extreme rapidity of human intellectual evolution, and the speed of advance of man's intelligence beyond that of his simian ancestors, in the geologically brief period of a million years, has been described by Eiseley as "an explosion of brains!" The genetic or anthropological changes that underlay the increment of a kilogram of brain, with a tripling of cerebral size, during hominid evolution through the Pleistocene Period, are still unknown. In particular, it does not yet seem possible to explain the feature that plagued Alfred Russel Wallace, *i.e.*, why most of this increment had already been attained at the stage of Neanderthal man, about 100,000 years in advance of any significant use that was made of it. Wallace's famous remark, made in 1869, was: "Natural selection could only have endowed the savage with a brain little superior to that of an ape; whereas he actually possesses one but very little inferior to that of the average member of our learned societies."

On the other hand, once modern man had acquired a competent brain, it is feasible to propose that his rapid intellectual advance rested upon the development of processes for evolution independent of those determined by genetic means. Modern man has found it possible to substitute, for phylogenetic modification, maturational changes in his brain acquired during the course of his individual, postnatal development. In this way, he has been able to avoid dependence upon variations reproductively transmitted through a series of generations, with preservation of favored ones by natural selection working over long intervals of time.

The deferral of maturation of the higher parts of his brain until after birth is among the most important of the factors by which modern man has, to this degree, become independent of the processes of biological evolution. In spite of a long gestation period of 38 weeks, typical of the great apes (chimpanzee, 34 weeks; orang, 39 weeks), each human infant is exceedingly immature at birth, particularly with respect to his higher neural functions and most of all those of the cerebral hemispheres, whose cortex provides the all-important organ for his maturation. Delay of cerebral growth to the postnatal period is advantageous also in the respect that man's brain is already so large at parturition as just to permit uninjured passage through the birth canal.

In the early postnatal period, growth of man's brain is more rapid than that of any other organ of the body. His brain weight doubles (from 380 to 630 gm.) in the first 6 months after birth, and more than doubles again (from 630 to 1,330 gm.) by the age of 4 years. Further increment is slight but the brain's full weight is not reached until the age of 20. While this gain is quantitative testimony for the pronounced and prolonged maturation of the brain after birth, no direct relationship can be drawn between it and the rise of functional neural capacity during individual development. For example, man's intellectual attainment is much greater between the ages of 4 and 20 years, when the weight of his brain increases only 120 gm., than during the first 4 years of life, when the brain expands by almost a kilogram. Furthermore, the ratio of brain to body weight diminishes rather than rises during postnatal growth for, while the brain increases four times by adulthood, the weight of the body has increased twenty times, or five times as much.

Maturation of the brain's functional capacity is related more to the increase of its cytological than to its gross complexity. These microscopic alterations, in which weight changes are minimal, involve the elaboration of dendritic processes of neurons; the development of new or preferential pathways and synapses associating previously unrelated parts; the rise of shifting foci of neural facilitation or inhibition, grading central activity; the formation of loop circuits and feed backs modifying neural input and output; and the capacity, whatever its basis, by which previous activity in the nervous system can later be reinvoked, as memory, to merge with and influence current action.

In addition to these general features, more organized developments in the maturing brain lead to the formation of elaborate cortical receiving areas for each of the sensory modalities, to which all incoming information is relayed, and whose activity underlies subjective perception. Reciprocally, because the only way the brain can express itself is through motor performance, a cortical area develops which subserves "voluntary" movement of the body parts. In the monkey, no one of the parts of the body has a markedly greater representation in this motor cortex than the others, and this is in keeping with the absence of any pronounced regional specialization in the general motor performance of subhuman primates.

In man, by contrast, the hand has come to assume an almost exclusive role in all skilled, dextrous, manipulative activity. Its opposable thumb, in particular, forms man's chief prehensile organ. Correspondingly, in man a much larger area of motor cortex is devoted to representation of the hand, especially the thumb, than to that of the rest of the arm, trunk, and leg. Furthermore, in man, one of the two hands, most often the right, characteristically develops a greater proficiency and comes to be used more frequently than the other. This handedness is associated with a dominance of the opposite cerebral hemisphere, because the motor paths are crossed; in a right-handed individual, the left hemisphere is the dominant one.

In man, the face, tongue, and larynx also have an extensive representation in the motor cortex, equivalent in area to that of the hand. Just as the use of the hand in complex acts, such as making or using tools, involves the cortical region ahead of the arm area proper, so the performance of the lips, tongue, and larynx in vocal speech has come to be managed by the cortical region ahead of the face area of the motor cortex. Unlike other motor representation in the brain, this special capacity for the production of sounds as symbols develops only in the dominant one of the cerebral hemispheres. In analogous relation to the cortical sensory areas for hearing and for vision, further special capacities develop for the recognition of auditory or visual signals as symbols, *i.e.*, for the recognition of spoken or written language. Lesions in these speech areas of the dominant hemisphere result in aphasia; analogous injury to the opposite side of the brain is without this consequence.

Obviously the phylogenetic development of the sensory and motor regions of the cortex and, in the dominant hemisphere, of the areas for speech and language, have been of major significance in the evolution of modern man. Knowledge of the stages of their development would be of the greatest possible interest for anthropology. Regrettably, the brain is the softest organ in the body and its preservation after death is brief. On the other hand, its protective and supportive bony case, the cranium, has the highest preservation index of any of the body parts, except for the teeth and jaw. Fossil crania form the common currency of physical anthropology, and measurement of their capacity provides valuable information of the gross dimensions of the brain. Endocranial casts have sometimes shown frontal and temporal convolutional patterns in remarkable detail, but further efforts to establish stages of differentiation of functional cortical areas from them have invariably and, it would appear, correctly been contested. The great interest in the subject shares with the limitation of real data in accounting for the many speculative proposals which have been advanced concerning the evolution of man's brain. One of the most common of them is the proposal that man's capacity for speech evolved from abilities for emotional vocalization present in lower animals.

Animal studies suggest that vocalization in emotional expression is managed by a neural mechanism in the middle brain stem, and data from clinical neurology support the presence of such a subcortical emotional mechanism in man as well. No functional relationship is known between this deep-lying mesencephalic system for emotional vocalization, widely present through the animal kingdom, and the topographically distant cortical areas for symbolic speech, which exist only in the associational cortex of the human brain. In keeping with their phylogenetic difference, these two mechanisms for vocal communication display widely different maturation times in the ontogeny of the human infant. As might be expected, the older, more stereotyped, subcortical, emotional mechanism is fully functional at birth. By contrast, in the infant, activity of the cortical mechanism for symbolic speech is only manifest about 6 months later, as the incomprehensible babbling and jabbering, described as vocal play. Its function in understandable speech only develops between 1 and 2 years after birth. Its capacities in written language are not gained until the child is 5 or 6 years of age.

These observations oppose the view that man's capacity for speech evolved from the abilities for emotional vocalization present in lower animals. On the contrary, man's communication by symbols, both vocal and written, appears to represent an entirely novel functional increment, related to the acquisition of associational cortex, in front of the face and hand parts of the motor area, in the case of speaking and writing, and around the cortical sensory areas for audition and vision, in the case of recognition of spoken and written language. Man's capacities for communicating by symbolic language are unique also in depending upon neural mechanisms which develop only in the dominant one of the two cerebral hemispheres, rather than bilaterally.

These observations are in full agreement with Huxley's remarks, in *Evidence as to Man's Place in Nature*, in 1863: "Our reverence for the nobility of manhood will not be lessened by the knowledge that man is one with the brutes; for he alone possesses the marvellous endowment of intelligible and rational speech, whereby, in the secular period of his existence, he has slowly accumulated and organized the experience which is almost wholly lost with the cessation of every individual life in other animals."

### POSTNATAL MATURATION OF MAN'S BRAIN

The large balance of the cerebral cortex, outside of these more specifically preoccupied regions, is called associational because of its involvement with the more abstract, conceptual and ideational aspects of intellectual life. These complex functions bear a general relation to the bulk of the brain, in the sense that a large mass of neural tissue is required for their performance. Capacities in this direction increase through the phylogenetic series as the brains of animals become progressively larger. Furthermore, within man's own cerebrospinal nervous system, increasing complexity of function is encountered on moving cephalically along the neuraxis. Intrinsic function of the small spinal cord is primarily reflex in nature. That of the somewhat stouter brain stem is more elaborate, but it is still concerned largely with preserving internal homeostasis. It is primarily within the robust cerebral hemispheres, forming the main bulk of the brain, that the higher neural functions that relate man to the external world and to his fellows in it have their seat.

Without evoking the biogenetic law and recognizing that increments of weight bear only the most general and potential relationship to functional capacity, it is of interest to compare the stages of postnatal growth of the human infant's brain with the adult dimensions of earlier forms. At the age of 1 month, the weight of the human infant's brain (460 gm.) is about that of adult apes. At 3 months, his brain (550 gm.) is the size of that of the African man-apes. At 11 months, when the modern infant is first beginning to talk, his brain (850 gm.) equals that of Java man. At the age of 3 years, when he has learned to talk fairly well, his brain (1,110 gm.) is about the weight of that of Peking man; at the age of 10, the weight of the infant's brain (1,410 gm.) matches that of Neanderthal man and is essentially fully grown.

In man's capacity to substitute individual development for phylogenetic evolution, deferral of his cerebral maturation is matched in relevance by the great prolongation of each of the main periods of his postnatal life. While the duration of man's prenatal period is about the same as that of the great apes, the period of his postnatal growth has almost doubled, and his total life span is also twice that of simians. General growth is completed in 3 years in prosimians (shrews, lemurs, and tarsiers), 7 years in catarrhine monkeys, 11 years in great apes; in man, however, this period has increased to 20 years. Similarly, the total life span has grown from 25 years in monkeys to about 35 years in apes to over 70 years in modern man. While man's gestation period is not unique, except for being inadequate for his cerebral maturation, he is markedly specialized in the great prolongation of his postnatal growth and in his long postponement of the onset of senility.

As a consequence of these factors—postponement of man's cerebral maturation and the prolongation of his total life—development of the cerebral portion of his brain and its functions may be extended over a third or more of his existence. Instead of proceeding in an immutable fashion, isolated within the uterus and subject only to genetic blueprinting and the stereotyped environment of the maternal circulation, development of the cerebral part of man's brain is transported into a setting in the external world, where it becomes subject to all the parental, familial, and other interpersonal influences of modern man's social environment, as well as to features of his cultural heritage accumulated during a civilization of several thousand years.

While this individual, postnatal evolution of man's brain proceeds gradually, two clear periods can be distinguished in it. The first 2 years after birth are devoted largely to the perfection of general sensorimotor performance. From the age of 2 to 6, however, the ability to communicate by speech and writing is perfected and, thereafter, the speed of intellectual development rises precipitously. The human neonate can awaken, vocalize upon discomfort, suckle, display tonic neck reflexes related to the posture of the head, and show generalized startle reactions upon novel stimulation. This initial, stereotyped behavior is much like that of surviving anencephalic infants lacking a cerebral cortex. Increasingly, however, the human infant develops capacities related to the rise of cortical function.

His functional maturation proceeds cephalocaudally. At 3 months, he is able to focus and track visually, and a rhythm appears in his electroencephalogram, though a further period is needed before adult $\alpha$-frequency and amplitude are attained. At 4 months, the infant can reach and grasp; at 11 months, he can creep and stand; and at 15 months, he can walk alone. Talking develops between the ages of 1 and 2 years, and the child begins to read and write at 6. Its further manipulation of symbols extends rapidly, and formal education in organized fields of knowledge usually continues until adolescence or longer. Indeed, most of us cherish the notion that we can continue to learn and improve intellectually until senility sets in, after which we are convinced of it.

In association with the functional immaturity of man's brain at birth, and along with its gradual acquisition of increasingly complex capacities, have developed the various means by which the human infant is sheltered, nourished, protected, and educated during his maturation. The period of infant dependency is 1 year in monkeys, 2 years in apes, and 6 to 8 years in modern man. Freud has remarked that the lengthy dependence of the human child upon its parents is an overwhelmingly important biological fact. Consideration of the prolonged maturational processes, leading to acquisition of intelligence, is thus of basic significance in accounting for the rapid evolution of brain function in modern man.

Of the closest relationship also is modern man's Lamarckian attainment of the ability to transmit his acquired characteristics into the future, and again by neural rather than by genetic processes. Man had found it possible, as a substitute for mutational variations transmitted by genes and chromosomes with selection pressures determining survival, to apply processes of higher nervous activity to the creation of novel ideas, concepts, and discoveries, and has developed a written language and a body of learning related to it, by which his intellectual heritage can be conveyed to future members of his race. The brain has thus come to form the chief organ responsible both for man's rapid evolutionary advance and for the perpetuation of his culture.

This neurally determined evolution of modern man has proven fantastically more rapid and, in some ways, remarkably superior to that dependent upon reproductive and genetic processes. It does not appear, however, that a continued increase in the size of the brain is to be anticipated. Von Bonin has concluded from his studies that "while the human brain is larger than that of our subhuman ancestors, no further increase has taken place since the time of Neanderthal man, and there is definite indication of a decrease, at least in Europe, within the last 10,000 or 20,000 years. All these facts suggest that size of the brain has become stable, its evolutionary path has turned a corner, and internal organization rather than bulk appears now to be of positive selective value." In considering the situation, Eiseley states: "We do not have to abandon natural selection as a principle, but it is obvious that we must seek selective factors of a sort that Darwin never envisaged, and which may be bound up with speech and social factors difficult to investigate paleontologically." Schultz has commented: "The study of mankind's past has been largely in the domain of the physical anthropologist; our future evolution represents chiefly a problem for the social anthropologist. Man's future evolution is likely to be less dependent on physical than upon psychic perfection."

## REFERENCES

ARIENS KAPPERS, C. U.: The fissures on the frontal lobes of *Pithecanthropus erectus Dubois* compared with those of Neanderthal men, *Homo recens* and Chimpanzee. *Proc. Sect. Sc. K. Akad. Wetensch. Amsterdam* 32, *182-195 (1929).*

———: The fissuration on the frontal lobe of *Sinanthropus pekinensis Black*, compared with the fissuration in Neanderthal men. *Proc. Sect. Sc. K. Akad. Wetensch. Amsterdam* 36, pt. 2, *802-812 (1933).*

———: Further communication on the fissures of the frontal lobes in Neanderthal men. *Proc. Sect. Sc. K. Akad. Wetensch. Amsterdam* 32, pt. 1, *196-205 (1939).*

BAILEY, P., and VON BONIN, G.: *The Isocortex of Man.* Illinois Monogr. Med. Sc. 6, No. 1-2, 1951.

BAILEY, P., VON BONIN, G., and McCULLOCH, W. S.: *The Isocortex of the Chimpanzee.* Urbana, Univ. of Illinois Press, 1950.

BASS, A. D. (Ed.): *Evolution of Nervous Control from Primitive Organisms to Man.* Washington, American Association for the Advancement of Science, Publ. No. 52, 1959.

BATAILLE, G.: *Prehistoric Painting; Lascaux; or The Birth of Art.* Lausanne, Skira, 1955.

BAYLEY, N.: On the growth of intelligence. *Am. Psychol.* **10**, *805-818 (1955).*

BLACK, D.: On a lower molar hominid tooth from the Chou-Kou-Tien deposit. *Paleontologia sinica,* Ser. D, v. 7, fasc. 1, *1-28 (1927).*

———: The Croonian Lecture. On the discovery, morphology and environment of *Sinanthropus pekinensis. Phil. Trans. Roy. Soc. London* **B 223**, *57-120 (1934).*

BLACK, D.,*et al.*: Fossil man in China. *Mem. Geol. Surv. China.* Ser. A., No. 11 *(1933).*

BONIN, G. VON: On the size of man's brain as indicated by skull capacity. *J. Comp. Neurol.* **59**, *1-28 (1934).*

BOULE, M., and ANTHONY, R.: L'encéphale de l'homme fossile de la Chapelle-aux-Saints. *Anthropologie, Paris* **22**, *129-196 (1911).*

BOULE, M., and ANTHONY, R.: Neopallial morphology of fossil men as studied from endocranial casts. *J. Anat.* **51**, *95-102 (1917).*

BOULE, M., and VALLOIS, H. V.: *Fossil Men.* New York, Dryden Press, 1957.

BRAIDWOOD, R. J.: *Prehistoric Man.* 3rd Ed., Issued in co-operation with the Oriental Institute, University of Chicago. Chicago, 1957.

BROCA, P.: Sur les crânes et ossements des Eyzies. *Bull. Soc. Anthrop. Paris,* Ser. 23, *350-394 (1868).*

BROOM, R., and ROBINSON, J. T.: Sterkfontein ape-man Plesianthropus. Part I. Further evidence of the structure of the Sterkfontein ape-man *Plesianthropus. Transv. Mus. Mem.* **4**, pt. 1 *(1949).*

———: Swartkrans ape-man, *Paranthropus crassidens. Transv. Mus. Mem.* **6**, *1-123 (1952).*

BROOM, R., and SCHEPERS, G. W. H.: The South African fossil apemen, the *Australopithecinae.* Part I. The occurrence and general structure of the South African ape-men. *Transv. Mus. Mem.* **2**, *1-153 (1946).*

BROWN, T. G.: Note on the physiology of the basal ganglia and midbrain of the anthropoid ape, especially in reference to the act of laughter. *J. Physiol.* **49**, *195-207 (1914-15).*

BUCY, P. C. (ed.): *The Precentral Motor Cortex.* 2nd Ed. Urbana, Univ. of Illinois Press, 1949.

CLARK, G.: *From Savagery to Civilization.* New York, Schuman, 1953.

CONEL, J. L.: *The Postnatal Development of the Human Cerebral Cortex.* Cambridge, Harvard Univ. Press, 1939-55. (5 vols.)

DART, R. A.: *Australopithecus africanus*: the man-ape of South Africa. *Nature, London* **115**, *195-199 (1925).*

DART, R. A., and CRAIG, D.: *Adventures with the Missing Link.* New York, Harper, 1959.

DARWIN, C. R.: *The Descent of Man and Selection in Relation to Sex.* London, Murray, 1871.

DONALDSON, H. H.: *The Growth of the Brain: A Study of the Nervous System in Relation to Education.* London, Scott, 1895.

DUBOIS, E.: *Pithecanthropus erectus. Eine menschenaehnliche Ubergangsform aus Java.* Batavia, Landesdruckerei, 1894. *Jaarb. Mijnw. Nederl. Ind.* 24 *(Part 1), 5-77 (1895).*

———: *Pithecanthropus erectus,* eine Stammform des Menschen. *Anat. Anz.* 12, *1-22 (1896).*

———: The shape and size of the brain in *Sinanthropus* and in *Pithecanthropus. Proc. Sect. Sc. K. Akad. Wetensch. Amsterdam* 36 *(Part 1), 415-423 (1933).*

EISELEY, L.: Symposium commemorating the one hundredth anniversary of the discovery of Neanderthal man. I. Neanderthal man and the dawn of human paleontology. *Quart. Rev. Biol.* 32, *323-329 (1957).*

———: *Darwin's Century. Evolution and the Men Who Discovered It.* Garden City, N. Y., Doubleday, 1958.

ELLIOT SMITH, G.: *The Evolution of Man.* London, Oxford Univ. Press, 1924.

GESELL, A.: *The First Five Years of Life.* New York & London, Harper, 1940.

———: *The Embryology of Behavior.* New York, Harper, 1945.

GREENE, J. C.: *The Death of Adam. Evolution and its Impact on Western Thought.* Ames, Iowa State Univ. Press, 1959.

GREGORY, W. K.: *Man's Place Among the Anthropoids.* Oxford, Clarendon Press, 1934.

HAECKEL, E.: *The Evolution of Man.* New York, Appleton, 1896. (2 Vols.)

HALDANE, J. B. S.: Animal communication and the origin of human language. *Science Progress* 43, *385-401 (1955).*

HARRIS, J. A., *et al.*: *The Measurement of Man.* Minneapolis, Univ. of Minnesota Press, 1930.

HOWELL, F. C.: The Villafranchian and human origins. *Science* 130, *831-844 (1959).*

HOWELLS, W.: *Mankind in the Making.* Garden City, N. Y., Doubleday, 1959.

HURZELER, J.: *Oreopithecus bambolii* Gervais, a preliminary report. *Verhandl. naturf. Gesellsch. Basel.* 69, *1-48 (1958).*

HUXLEY, T. H.: *Evidence as to Man's Place in Nature.* London and Edinburgh, Williams and Norgate, 1863.

KEITH, A.: *The Antiquity of Man.* London, Williams and Norgate, 1925. (Revised Edition).

KELLY, A. H., BEATON, L. E., and MAGOUN, H. W.: A midbrain mechanism for facio-vocal activity. *J. Neurophysiol.* 9, *181-189 (1946).*

KOENIGSWALD, G. H. R., VON (ed.): *Hundert Jahre Neanderthaler,* *1856-1956;* Gedenkbuch der Internationalen Neanderthal, Frier, Düsseldorf, August 1956. Utrecht, Kemink en Zoon, 1958 (pp. 26-30).

LEAKEY, L. S. B.: A new fossil skull from Olduvai. *Nature, London* **184**, *491-493 (1959)*.

LEGROS CLARK, W. E.: *History of the Primates* . . . Fourth edition. London, Printed by order of the Trustees of the British Museum, 1954.

———: *The Fossil Evidence for Human Evolution* . . . Chicago, Univ. of Chicago Press, 1955.

LEGROS CLARK, W. E., and LEAKEY, L. S. B.: The Miocene *Hominoidea* of East Africa. Brit. Mus. (*Nat. Hist.*). *Fossil Mammals of Africa,* **1**, *1-117*, Illus. *(1951)*.

LYELL, C.: *The Geological Evidence of the Antiquity of Man.* London, Murray, 1863.

MOORE, R.: *Man, Time and Fossils.* New York, Knopf, 1953.

OAKLEY, K. P.: *Man the Tool-maker.* Chicago, Univ. of Chicago Press, 1957.

OSBORN, H. F.: *Men of the Old Stone Age.* 3rd Ed. New York, Scribner's Sons, 1919.

PENFIELD, W., and RASMUSSEN, T.: *The Cerebral Cortex of Man.* New York, Macmillan, 1950.

PENFIELD, W., and ROBERTS, L.: *Speech and Brain Mechanism.* Princeton, N. J., Princeton Univ. Press, 1959.

PIVETEAU, J.: *Traité de Paléontologie.* Vol. VII. *Primates; Paléontologie Humaine.* Paris, Masson, 1957.

PUMPHREY, R. J.: *The Origin of Language.* Liverpool, University Press, 1951.

ROBINSON, J. T., and MASON, R. J.: Occurrence of stone artifacts with *Australopithecus* at Sterkfontein. *Nature, London* **180**, *521-524 (1957)*.

SCHAAFHAUSEN, H.: Zur Kenntniss der altesten Rassenschädel. *Arch. Anat. Physiol. Jhrg. 453-478 (1858)*.

SCHEPERS, G. W. H.: The endocranial casts of the South African apemen. Part II. The South African fossil ape-men: the *Australopithecinae. Transv. Mus. Mem.* **2**, *154-272 (1946)*.

SHIRLEY, M. M.: *The First Two Years. A Study of Twenty-five Babies.* Vol. 2. *Intellectual Development.* Minneapolis, Univ. of Minnesota Press, 1933.

SPUHLER, J. N.: Somatic paths to culture. *Human Biol.* **31**, *1-13 (1959)*.

SPUHLER, J. N., *et al.*: *The Evolution of Man's Capacity for Culture.* Detroit, Wayne State Univ. Press, 1959.

STRAUS, W. L., JR.: The riddle of man's ancestry. *Quart. Rev. Biol.* **24**, *200-223 (1949)*.

STRAUS, W. L., JR., and CAVE, A. J. E.: Symposium commemorating the one hundredth anniversary of the discovery of Neanderthal man. III. Pathology and the posture of Neanderthal man. *Quart. Rev. Biol.* **32**, *348-363 (1957)*.

SYMINGTON, J.: Endocranial casts and brain form: a criticism of some recent speculations. *J. Anat. Physiol.* **50**, *111-130 (1916).*

TEILHARD DE CHARDIN, P.: *The Phenomenon of Man.* New York, Harper, 1960.

TILNEY, F.: The brain of prehistoric man. A study of the psychologic foundations of human progress. *Arch. Neurol. & Psychiat.* **17**, *723-769 (1927).*

———: *The Brain from Ape to Man . . .* New York, Hoeber, 1928 (2 Vols.).

VIERORDT, H.: Das Massenwachsthum der Körperorgane des Menschen. *Arch. f. Anat. u. Entwicklungsgesch.*, Suppl.-Bd., *62-94 (1890).*

WALLACE, A. R.: *My Life: A Record of Events and Opinions.* New York, Dodd, Mead & Co., 1905. 2 Vols.

WASHBURN, S. L.: The analysis of primate evolution with particular reference to the origin of man; *Origin and Evolution of Man. Cold Spring Harbor Symp. Quant. Biol.* **15**, *67-78 (1950)*

———: The new physical anthropology. *Tr. New York Acad. Sc.* Ser. II, **13**, *298-304 (1951).*

———: Speculations on the interrelations of the history of tools and biological evolution. *Human Biol.* **31**, *21-31 (1959).*

WASHBURN, S. L., and AVIS, V.: "Evolution of human behavior." *In Behavior and Evolution.* A. Roe and G. G. Simpson, Eds. New Haven, Yale Univ. Press, 1958 (pp. 421-36).

WEIDENREICH, F.: Observations on the form and proportions of the endocranial casts of *Sinanthropus pekinensis*, other hominids and the great apes: a comparative study of brain size. *Paleontologia sinica*, Ser. D, v. 7, fasc. 4 *(1936).*

——: The brain and its role in the phylogenetic transformation of the human skull. *Tr. Am. Philosoph. Soc.* n.s. **31** *(Part V), 320-442 (1941).*

———: The skull of *Sinanthropus pekinensis*; a comparative study on a primitive hominid skull. *Paleontologia sinica* n.s., D, 10 *(1943).*

WEIL, A.: Measurements of cerebral and cerebellar surfaces. Comparative studies of the surfaces of endocranial casts of man, prehistoric men and anthropoid apes. *Am. J. Phys. Anthropol.* **13**, *69-90 (1929).*

WEINER, J. S.: *The Piltdown Forgery.* London & New York, Oxford Univ. Press, 1955.

WENDT, H.: *In Search of Adam.* Boston, Houghton Mifflin, 1956.

WILSON, S. A. K.: *The Modern Problems in Neurology.* New York, Wood, 1929.

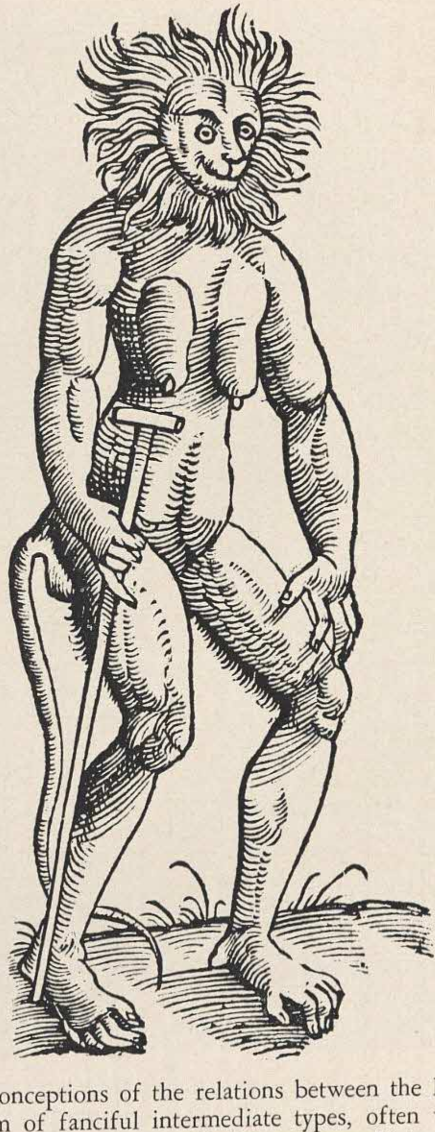

FIGURE 1. Early conceptions of the relations between the higher primates and man took the form of fanciful intermediate types, often with a mythological flavor. In this *Lucifer* from Aldrovandi (*Monstrorum historia.* Bononiae, 1642), the semierect posture, long tail, and suggestion of libidinousness emphasized bestial qualities that were presumed to contrast with the spiritual nature of contemporary man. In the famous tenth edition of his *Systema naturae* (1758), Linnaeus included man with his most similar contemporaries in the single order, Primates. In 1794, a thesis by his student, Hoppius, depicted *Troglodyta Bontu, Lucifer Aldrovandi, Satyrus Tulpii,* and *Pygmaeus Edwardi* among the *Anthropomorpha.*

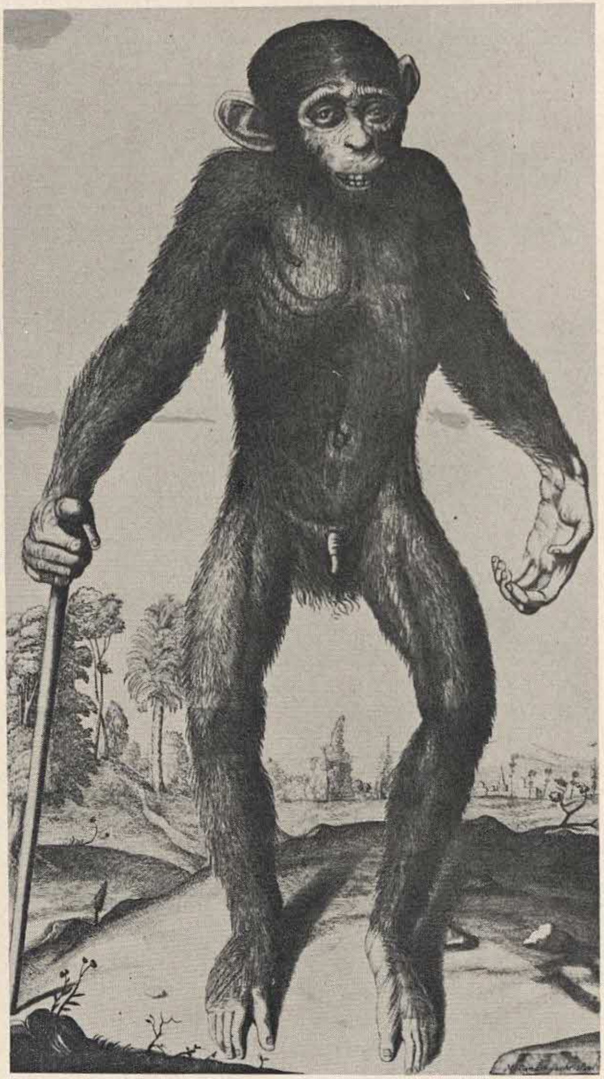

FIGURE 2. The seventeenth-century comparative anatomist, Edward Tyson, dissected the chimpanzee and placed it between monkey and man, thus contributing to the concept of "a missing link." The emerging clarity of the anthropoid's status is reflected in the title of Tyson's publication (London, 1699): "*Orang-outang*, sive *Homo Sylvestris*, or the Anatomy of a Pygmie compared with that of a monkey, an ape and a man. To which is added a Philological Essay concerning the *Pygmies*, the *Cynecephali*, the *Satyrs*, and the *Sphinges* of the Ancients, wherein it will appear that they are all either Apes or Monkeys, and not Men, as formerly pretended."

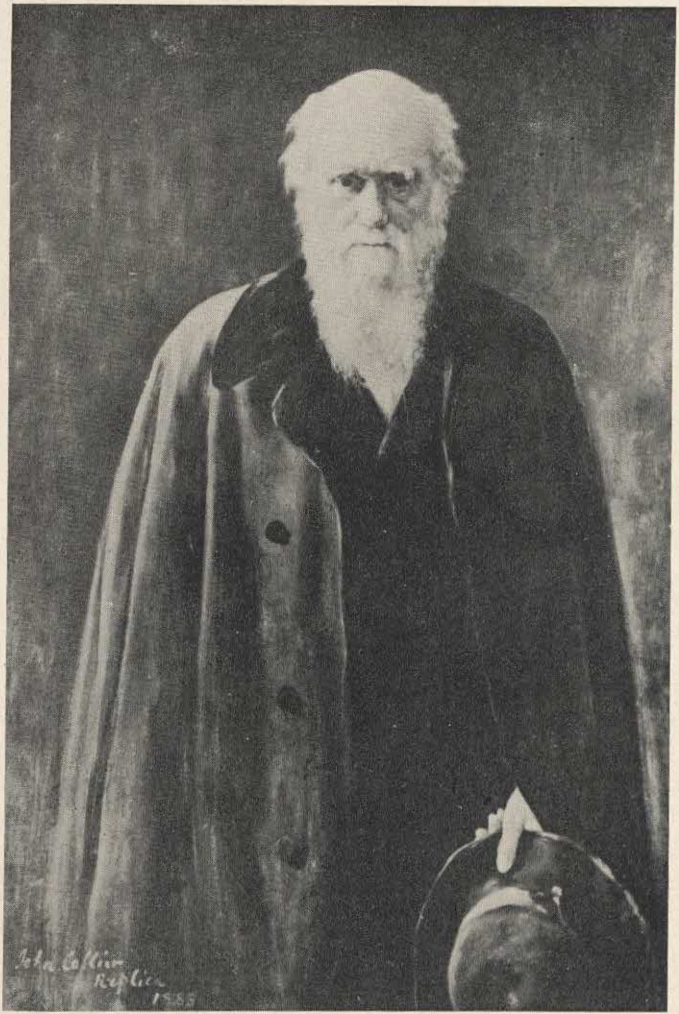

FIGURE 3. Charles Darwin's portrait, painted by John Collier, showed the elderly "Newton of Biology" as a sage-like figure, with black felt hat and cape, ready for his daily exercise on the Sand Walk at Downe. Darwin's early travels were distant memories. The storms aroused by the *Origin of Species* (1859) and his related psychosomatic illness had subsided, and Darwin had long since established a measured pattern of existence in his country home. In his *Descent of Man* (1871), Darwin wrote: "In each great region of the world, the living mammals are closely related to the extinct species. As the gorilla and chimpanzee are now man's nearest allies, it is somewhat more probable that our early progenitors lived on the African continent than elsewhere."

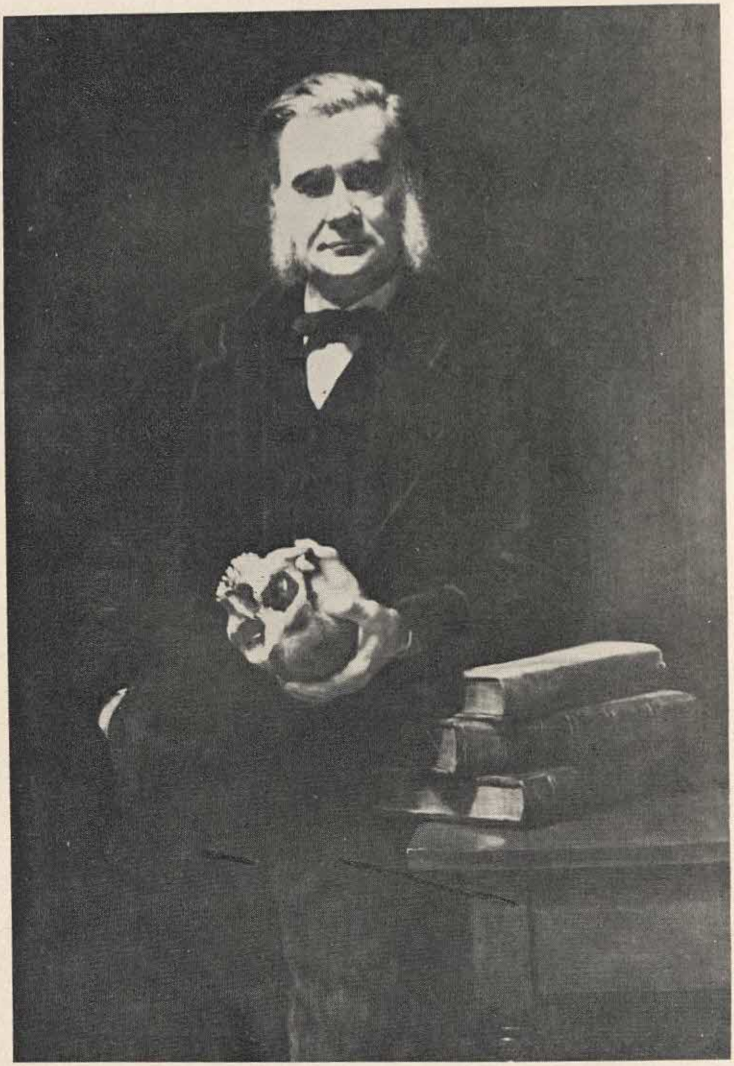

FIGURE 4. In Darwin's time, Thomas Henry Huxley was the most vigorous English protagonist of man's evolution from primate ancestry. His influential *Man's Place in Nature* (1863) concluded: "If the doctrine of progressive development is correct, we must extend by long epochs the most liberal estimate that has yet been made of the antiquity of man." The artist John Collier was twice Huxley's son-in-law and on each occasion painted his portrait. This one, in Hamlet pose, conveys the energetic pugnacity, the insightful clarity of mind, and the masterful capacity for expression that characterized this great expositor of biological science in the late nineteenth century.

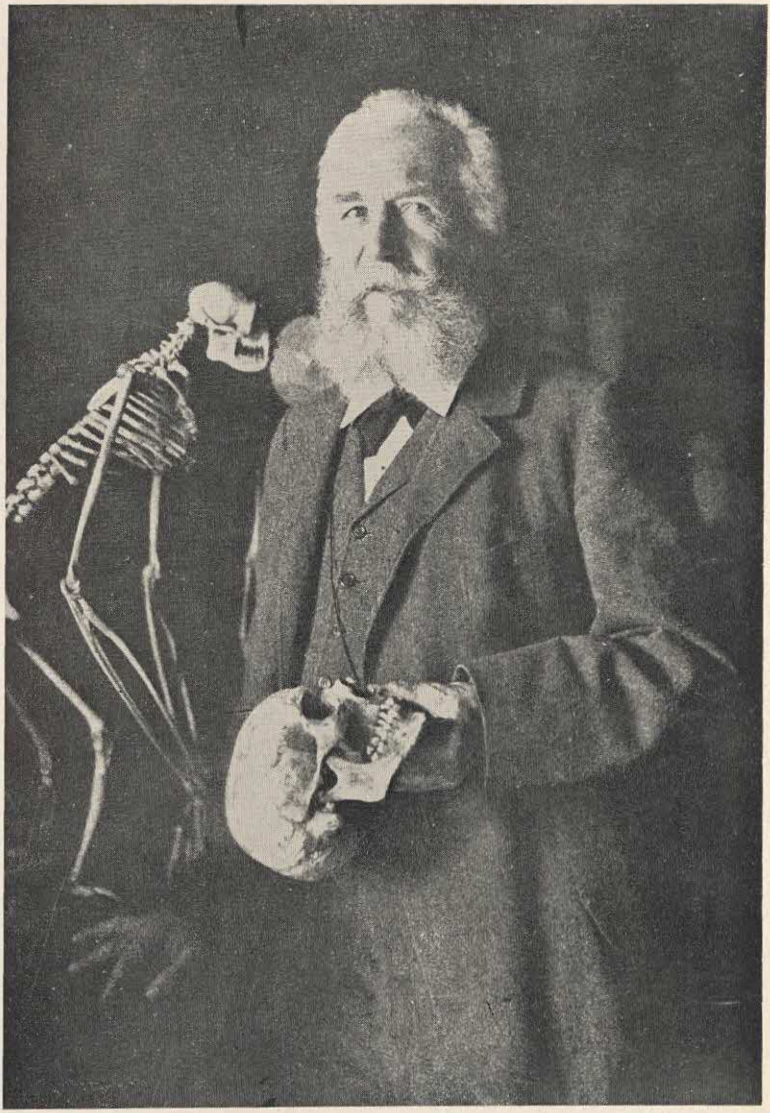

FIGURE 5. In this same period, Ernst Haeckel, Professor of Zoology at Jena, was the outstanding champion of Darwinism in Germany. Haeckel's studies of embryology led him to formulate the biogenetic law, that ontogeny recapitulates phylogeny. Additionally, because of their embryonic similarities, Haeckel proposed a gibbon- rather than an ape-like ancestor of man. Because the gibbon group is distributed in Indonesia rather than in Africa, Haeckel differed from Darwin in conceiving that man's evolution proceeded in a Paradise centered around the Indian Ocean, rather than in an African setting.

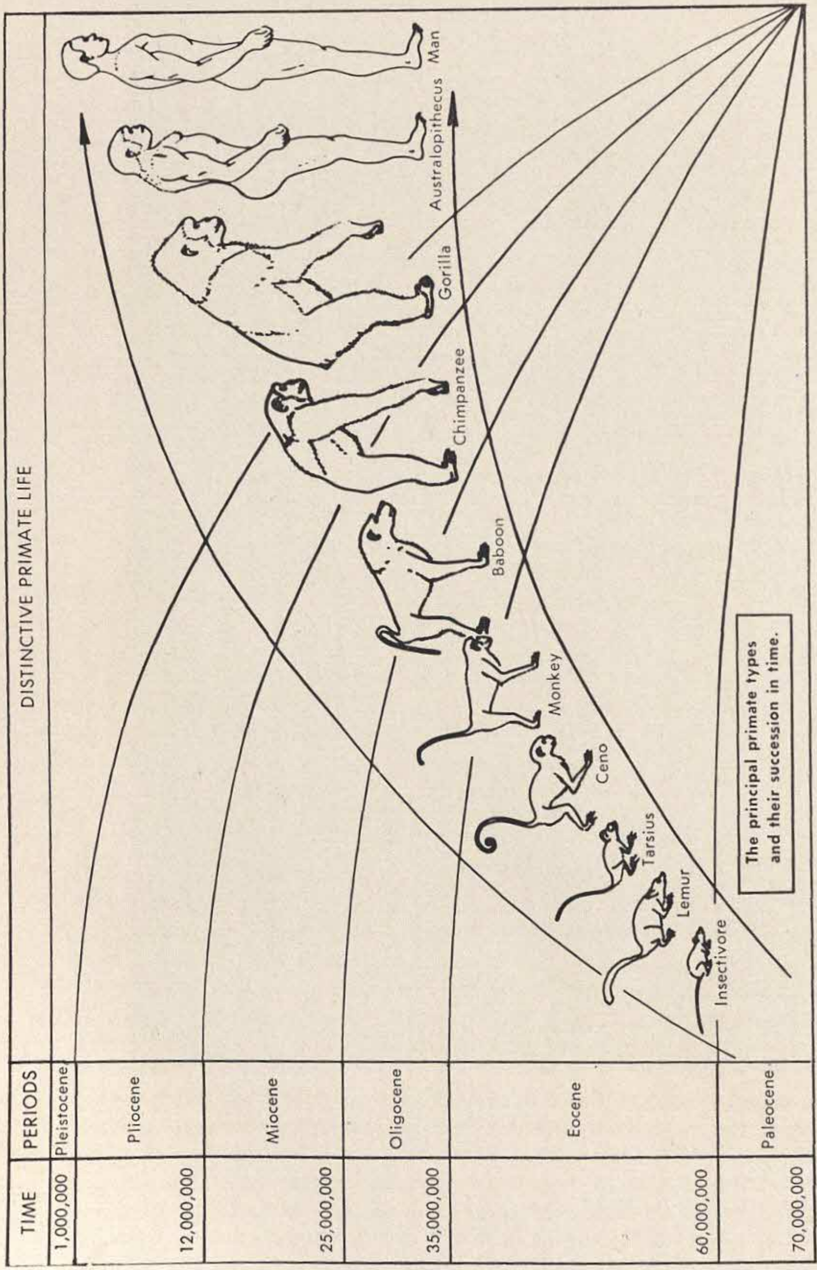

FIGURE 6. Two main schools of thought exist concerning man's evolution. The more popular "hat-rack" school proposes the radiation of many related species from a common source with extinction of all but present forms. The contrasting "candelabra" school follows the principle of parallelism and traces the coincident development of several separate lines of evolution from a distant common ancestor. Both agree upon the development, within the Primate order, of prosimians, monkeys, apes, and man, over a period proceeding from the Eocene, 60 million years ago, to the present. There is also concurrence that the interval during which man evolved is confined to the most recent fraction of this period, the Pleistocene, representing the last one million years. Reprinted from Dart, D. A.: *Adventures With the Missing Link*. New York, Harper. 1959.

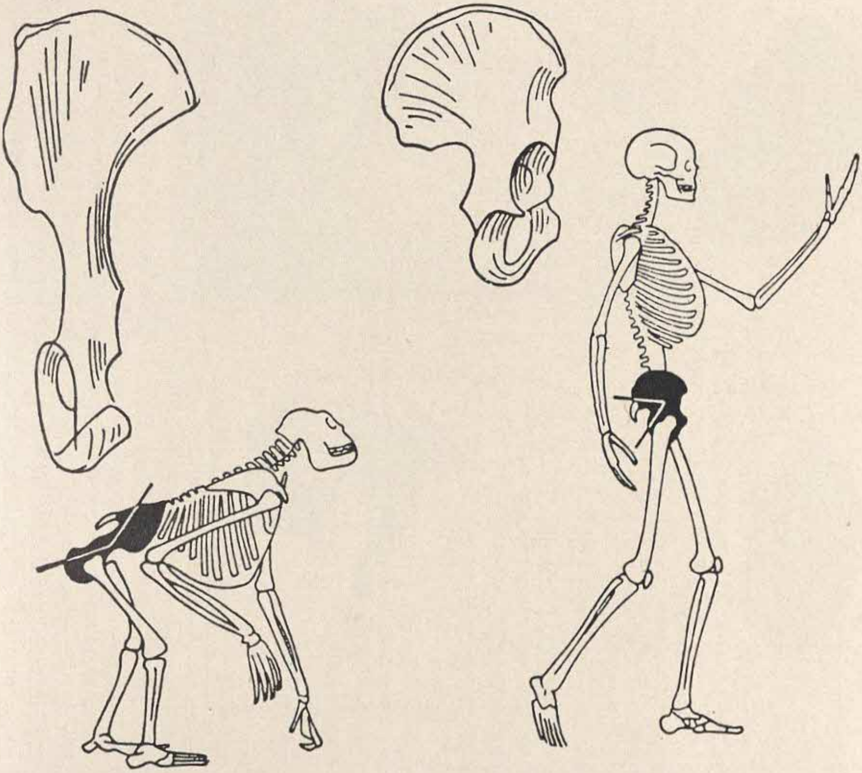

FIGURE 7. Of the three great body complexes involved in man's evolution, change in the pelvis and legs began his distinctive development. Acquisition of an upright posture and the ability to walk on his legs alone freed man's hands for the use of tools. Development of the third great complex, his brain, then followed. Apes, with a long slanting pelvis, can take only a few steps upright, and must use the hands to supplement their locomotion. With his shorter pelvis, man can stand and walk erect. Changes leading to an erect posture and to bipedal locomotion thus formed the first step in the evolution of man. Reprinted from Moore, R.: *Man, Time and Fossils.* New York, Knopf, 1953. (Plate drawn by Sue Richard).

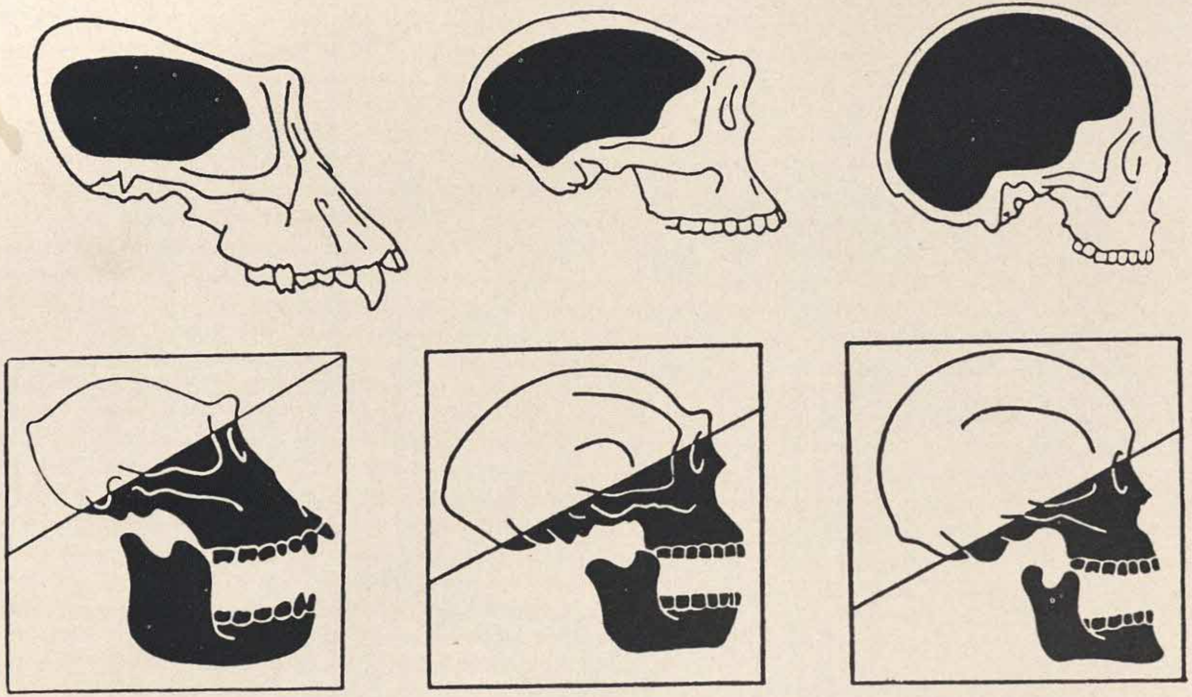

FIGURE 8. When man's hands became free from locomotory obligations, they began to develop prehensile and manipulative skills. With the manual assumption of many of the activities necessarily undertaken by the jaws of animals with quadrupedal locomotion, the massive development of the face, jaw and teeth regressed, and the various buttressing features of the skull, together with the expansion of its surfaces to provide increase in area for attachment of the powerful jaw musculature, gradually diminished in prominence. Associated with this progressive decrease in the lower part of the head was an expansion of the upper, cranial portion and an increment of its neural contents, the brain. These reciprocally shifting relations can be compared in the gorilla (left), *Pithecanthropus* (center), and modern man (right). Reprinted from Moore, R.: *Man, Time and Fossils*. New York, Knopf, 1953. (Plate drawn by Sue Richard).

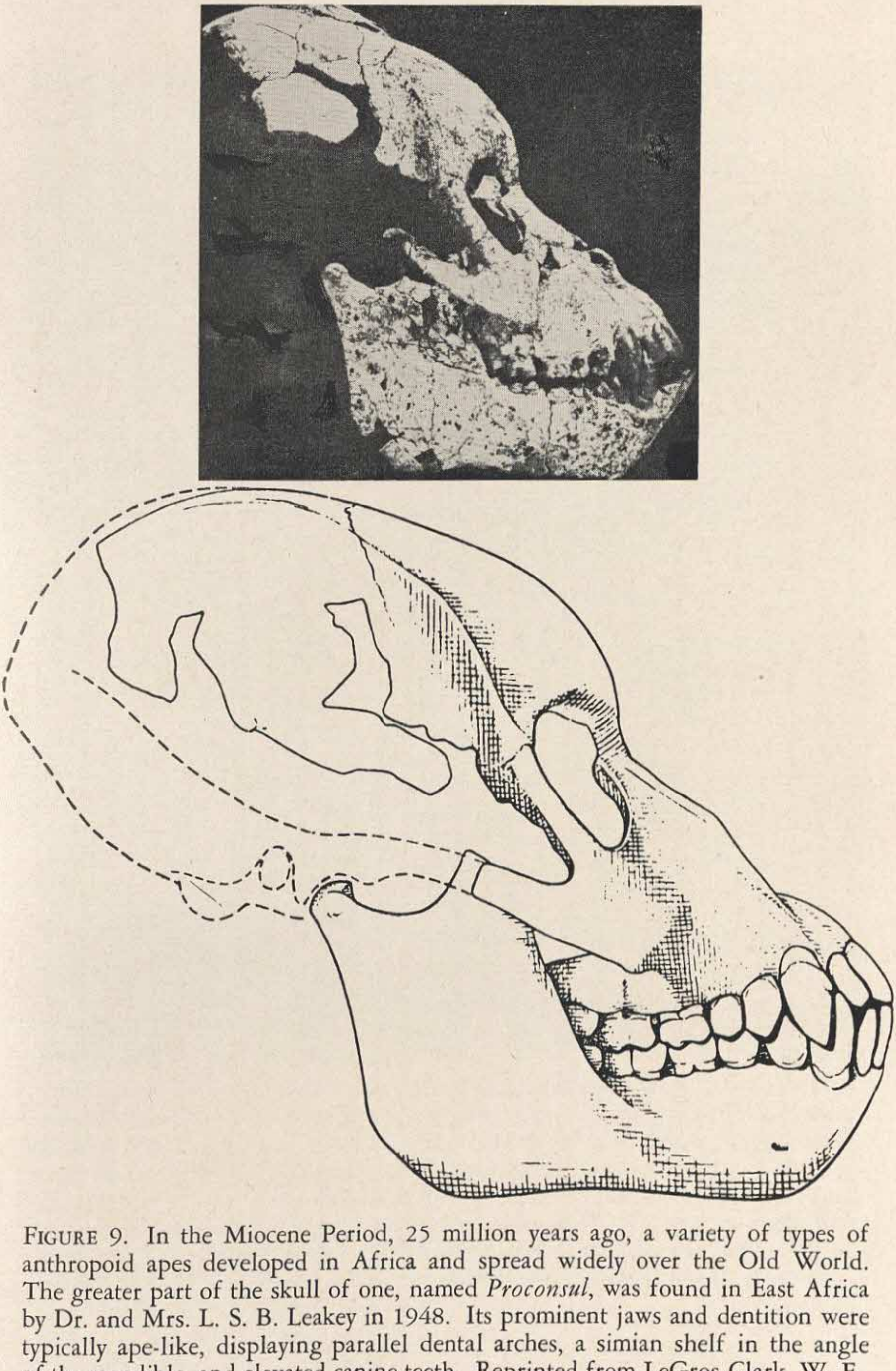

FIGURE 9. In the Miocene Period, 25 million years ago, a variety of types of anthropoid apes developed in Africa and spread widely over the Old World. The greater part of the skull of one, named *Proconsul*, was found in East Africa by Dr. and Mrs. L. S. B. Leakey in 1948. Its prominent jaws and dentition were typically ape-like, displaying parallel dental arches, a simian shelf in the angle of the mandible, and elevated canine teeth. Reprinted from LeGros Clark, W. E., and Leakey, L. S. B.: *The Miocene Hominoidea of East Africa*. London, British Museum, 1951.

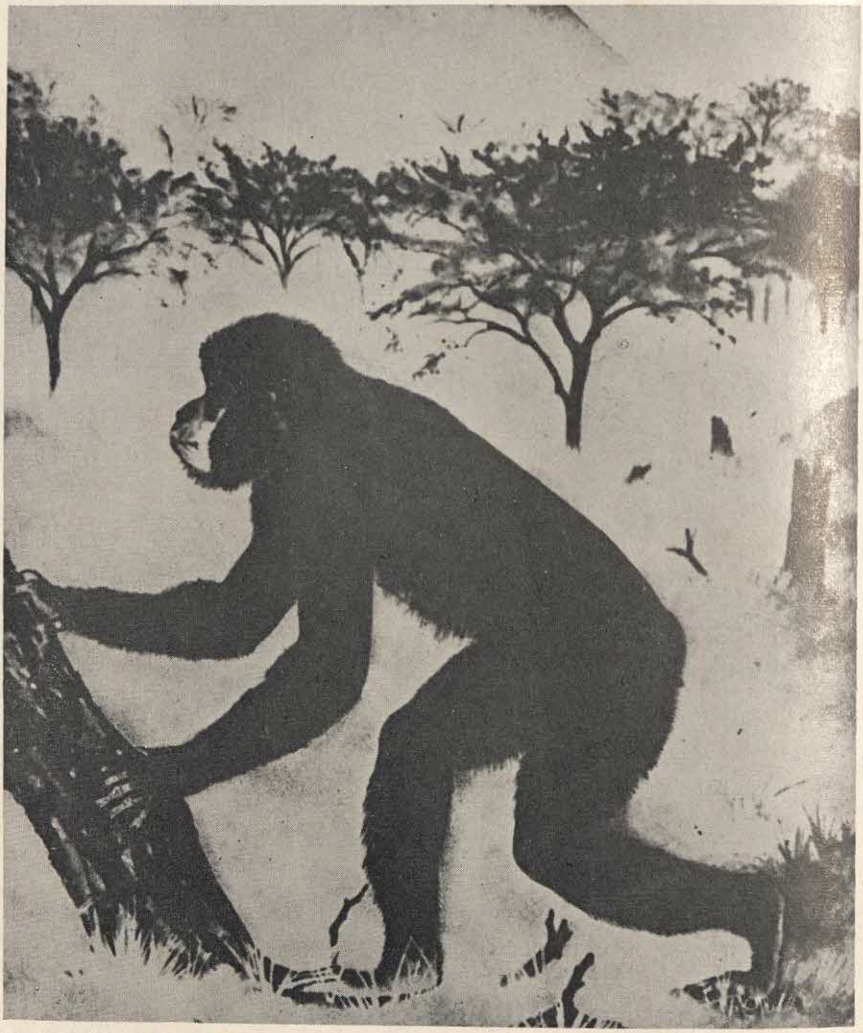

FIGURE 10. In an artist's conception, the terrain of these African Miocene apes consisted of wooded valleys separated by open country. Because of their size, *Proconsul* and related forms must have been restricted in their arboreal habits to the lower tree branches near the ground. It has been suggested that the adoption of bipedal locomotion was directed, not to the abandonment of arboreal life, but to an effort to retain it. In regions undergoing gradual deforestation, such an adaptation would enable an animal to cross intervening grasslands in its thinly wooded habitat. (A reconstructive drawing from the Museum of Natural History, London.)

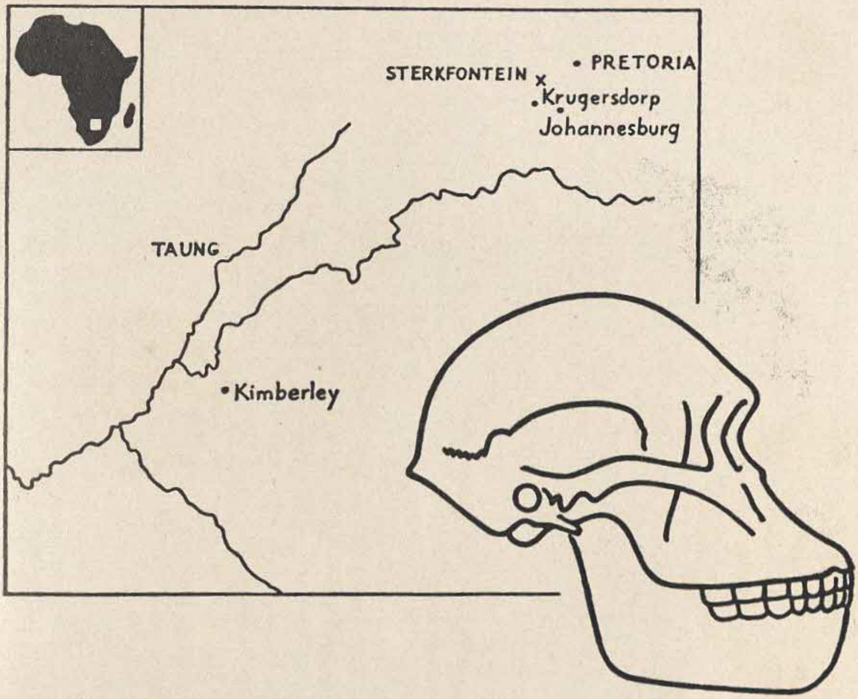

FIGURE 11. The Australopithecines, which formed the type hominid of the lower Pleistocene, were discovered in 1924 in Taung, near Kimberley, South Africa. Subsequent finds were made at Sterkfontein and other sites between Pretoria and Johannesburg. These African man-apes possessed a hominid pelvis and walked erect. They had begun to make and use crude tools. While their dentition was man-like, their faces and jaws were still prominently developed. Expansion of their crania was only minimal, and their brains were little larger than an ape's. Reprinted from Moore, R.: *Man, Time and Fossils*. New York, Knopf, 1953. (Plate drawn by Sue Richard).

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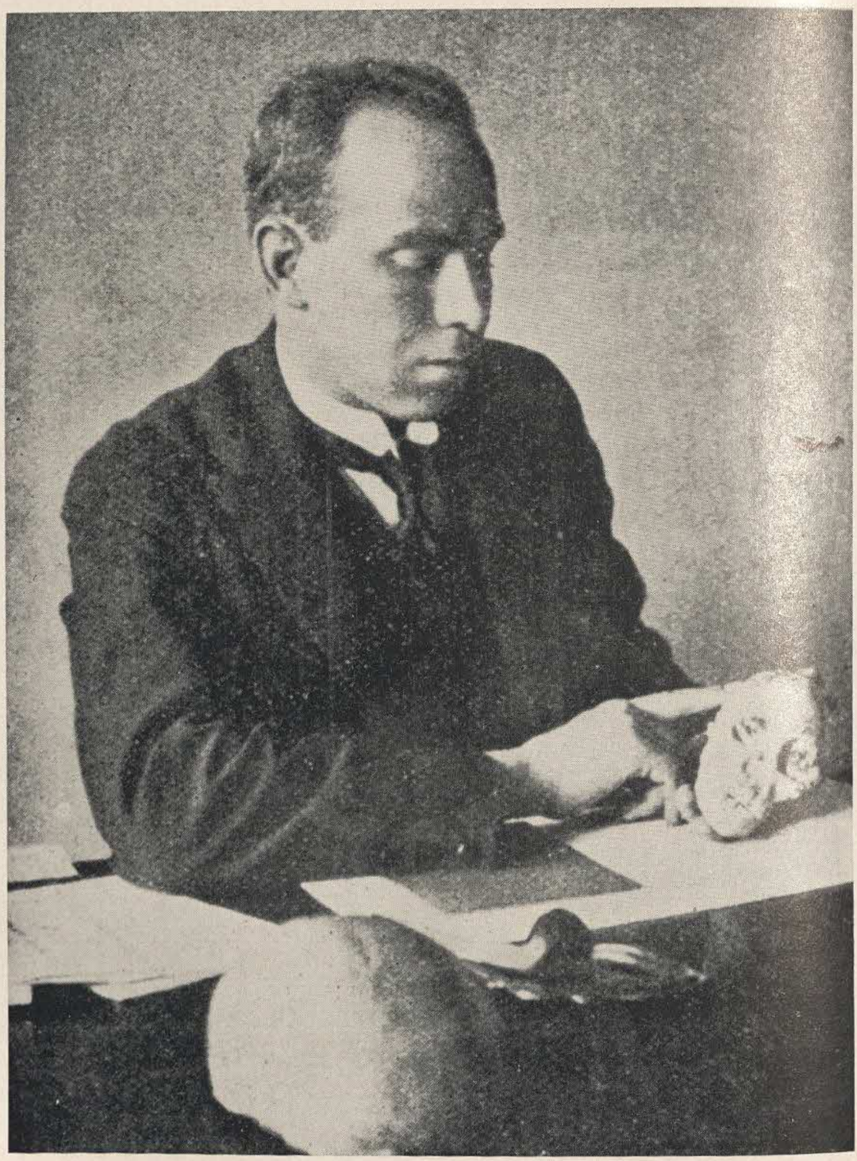

FIGURE 12. Professor Raymond A. Dart, Anatomist at the University of Witwatersrand, Johannesburg, was attracted by a fossil baboon skull presented to him by a medical student, and obtained further remains from the Northern Lime Company at Taung. He was here photographed in 1925 gazing pensively at the head of his great discovery, *Australopithecus*, with which hominid evolution began about a million years ago, in Africa, as Darwin had proposed.

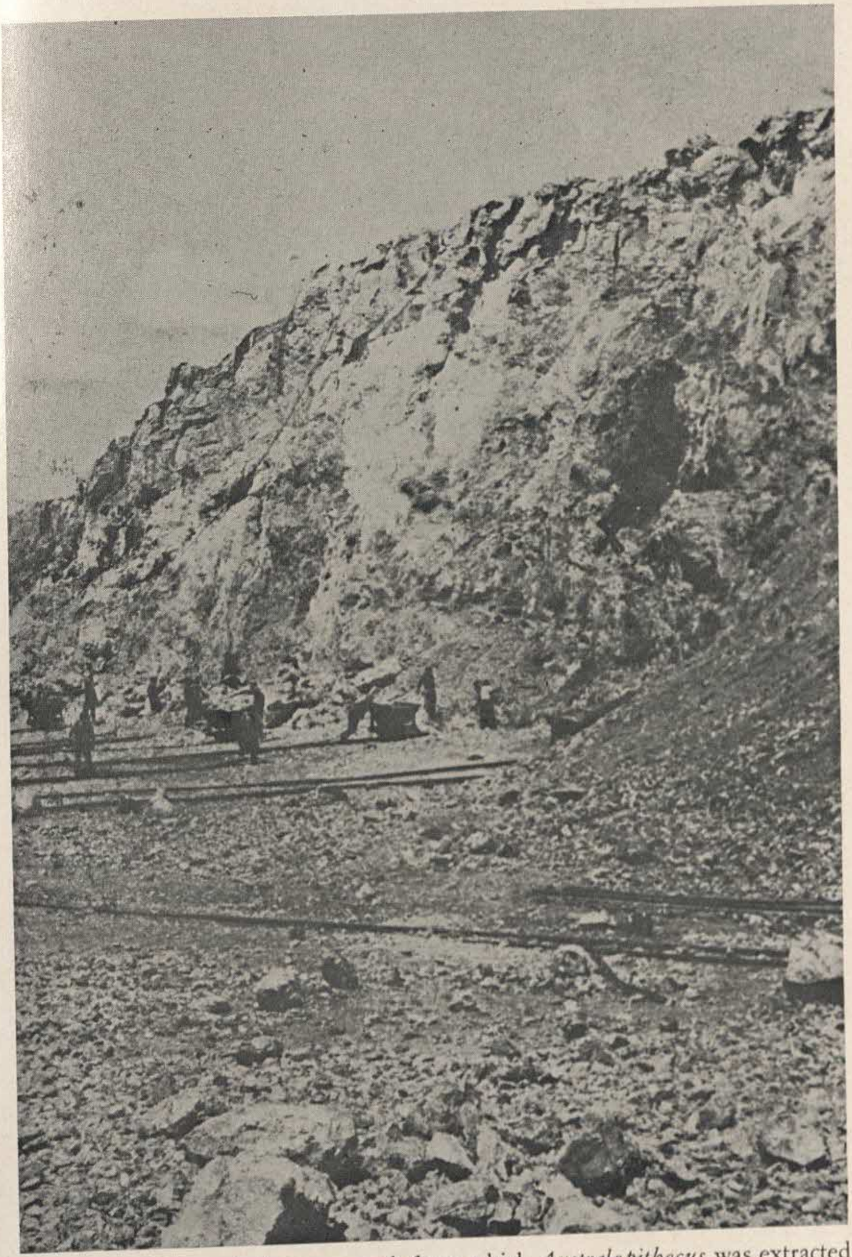

FIGURE 13. The sandy limestone rock from which *Australopithecus* was extracted came from this quarry at Taung, South Africa. The original site, long since destroyed by quarrying, was a cave filled with calcified breccia, backed up against a limestone cliff. Later, major remains were recovered from ancient caves in the low ridges bordering the broad valley between Swartskrans and Sterkfontein.

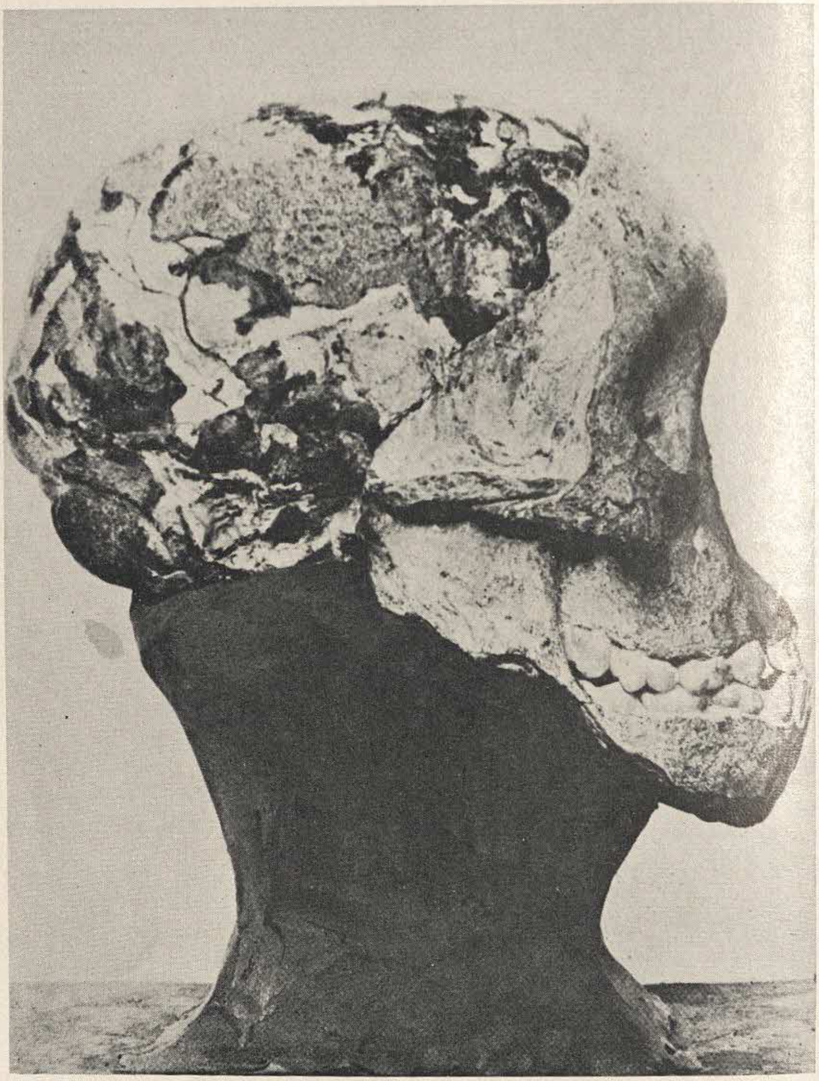

FIGURE 14. In his report of *Australopithecus* to *Nature* in 1925, Dart described the natural endocranial cast which "articulated exactly by its fractured frontal extremity with another piece of rock in which the broken left side of a mandible was visible. Careful development of the solid limestone in which it was embedded finally revealed almost the entire face." Most recently, Dart has written: "For my part, I am content to have participated in the opening of a few of the African doors into prehistory. Usually what helped me most was the agreement of a lot of other people that I was on the wrong track." Reprinted from Dart, R. A.: *Adventures with the Missing Link*. New York, Harper, 1959.

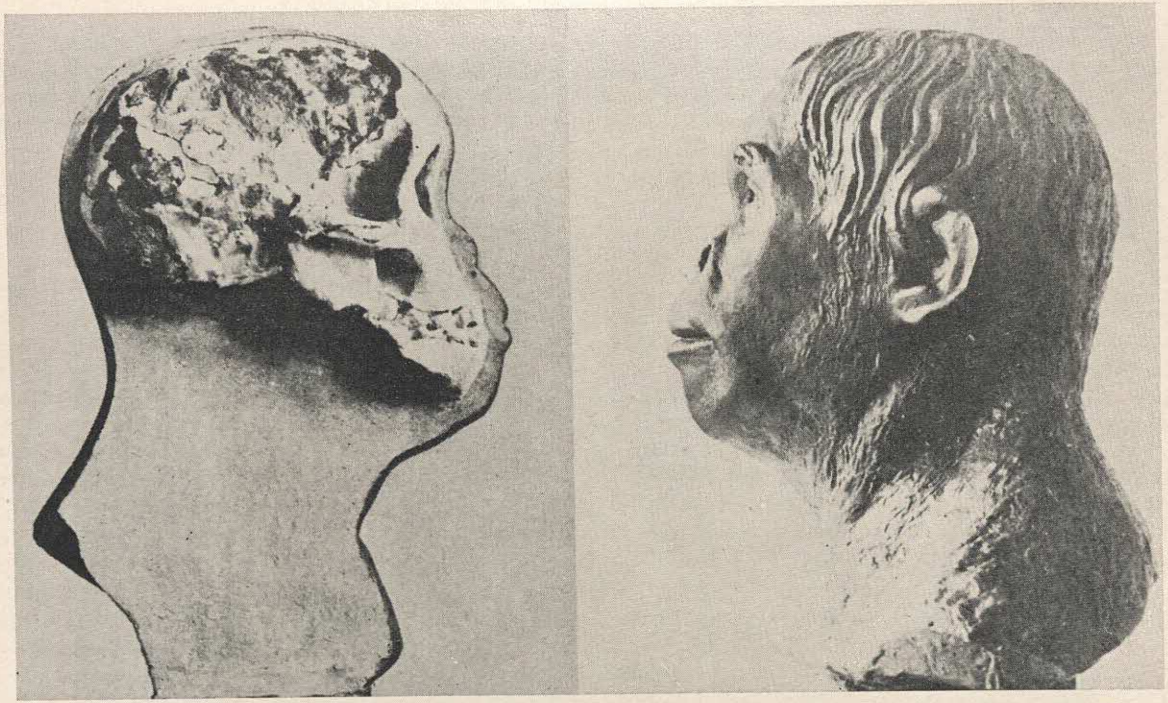

FIGURE 15. The infant *Australopithecus* reconstructed from the Taung skull was estimated to be a 5--year-old hominid, often since referred to as "Dart's baby." At an exhibition of Australopithecine reconstructions in New York in 1949, the anthropologist, Sherwood Washburn, remarked, "It looks as though these creatures were human from the neck down and anthropoid from the neck up." Their admixture of simian and hominid features can be categorized in terms of the sequential developments depicted in Figures 7 and 8. Pelvic changes leading to an erect posture had occurred, the hands were becoming manipulative, but the jaws still remained prominent and the brain had not yet enlarged. Reprinted from Dart, R. A.: *Adventures with the Missing Link*. New York, Harper, 1959.

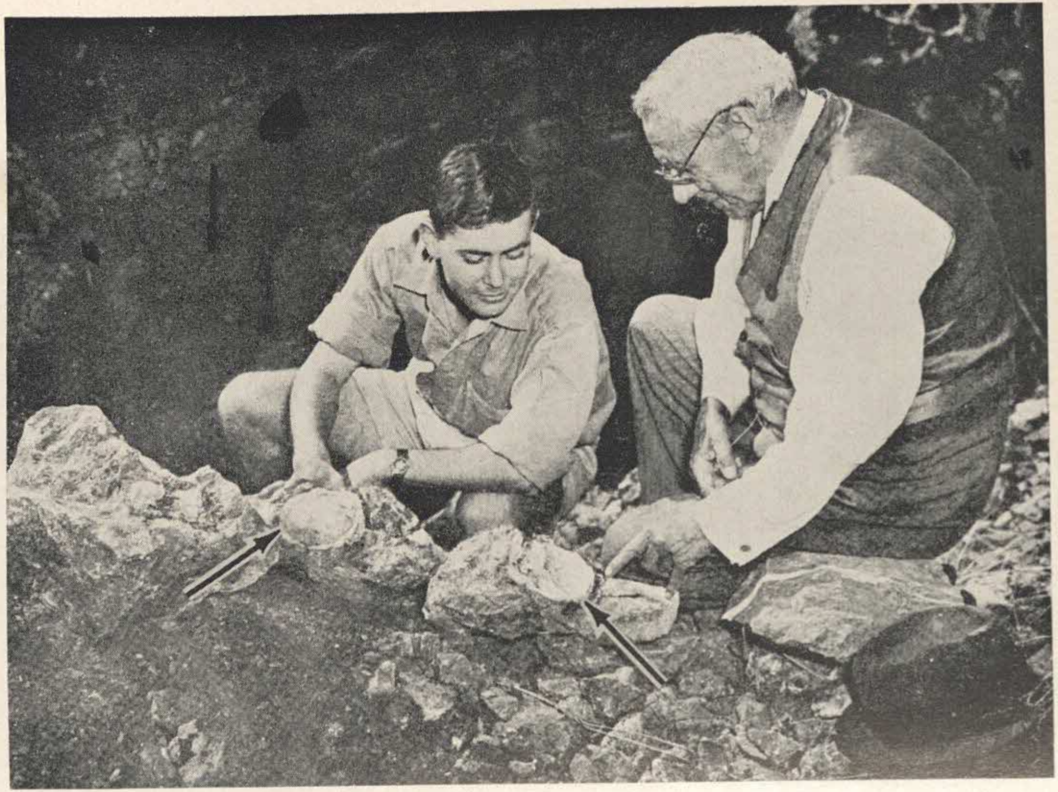

FIGURE 16. One of the most extraordinary finds in the search for early man occurred at Sterkfontein, Union of South Africa, in 1947, when Dr. Robert Broom and his assistant, John T. Robinson, recovered a perfect, whole skull of an adult Australopithecine. The calvarium at the left and the base of the skull at the right can both be seen in the center of the figure. In the excitement of the occasion, the usually impeccably dressed Dr. Broom is seen to have removed his hat and jacket.

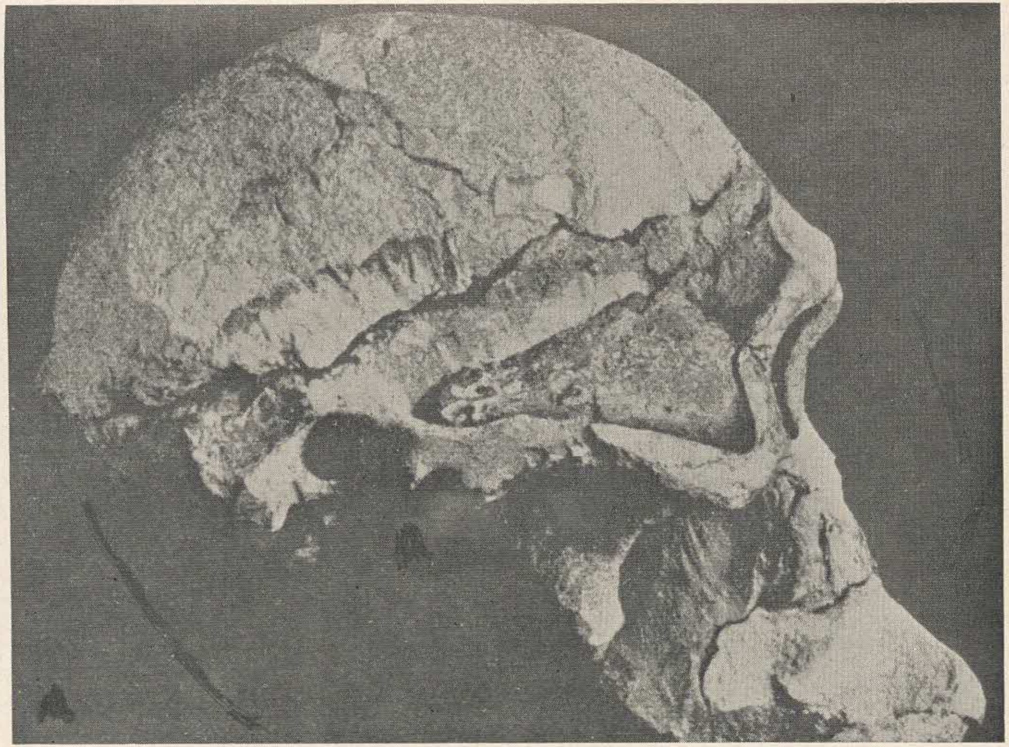

FIGURE 17. Lateral view of the perfect skull of a female Australopithecine, commonly known as Mrs. Ples (short for *Plesianthropus*), the discovery of which is shown in Figure 16. A complete innominate bone of this form demonstrated conclusively that the pelvic structure permitted an erect trunk and full extension of the legs in a stable, upright posture necessary for bipedal locomotion. Reprinted from Broom, R., and Robinson, J. T.: Further evidence of the structure of the Sterkfontein ape-man, *Plesianthropus. Transvaal Museum Memoirs*, 4, pt. 1, 1949.

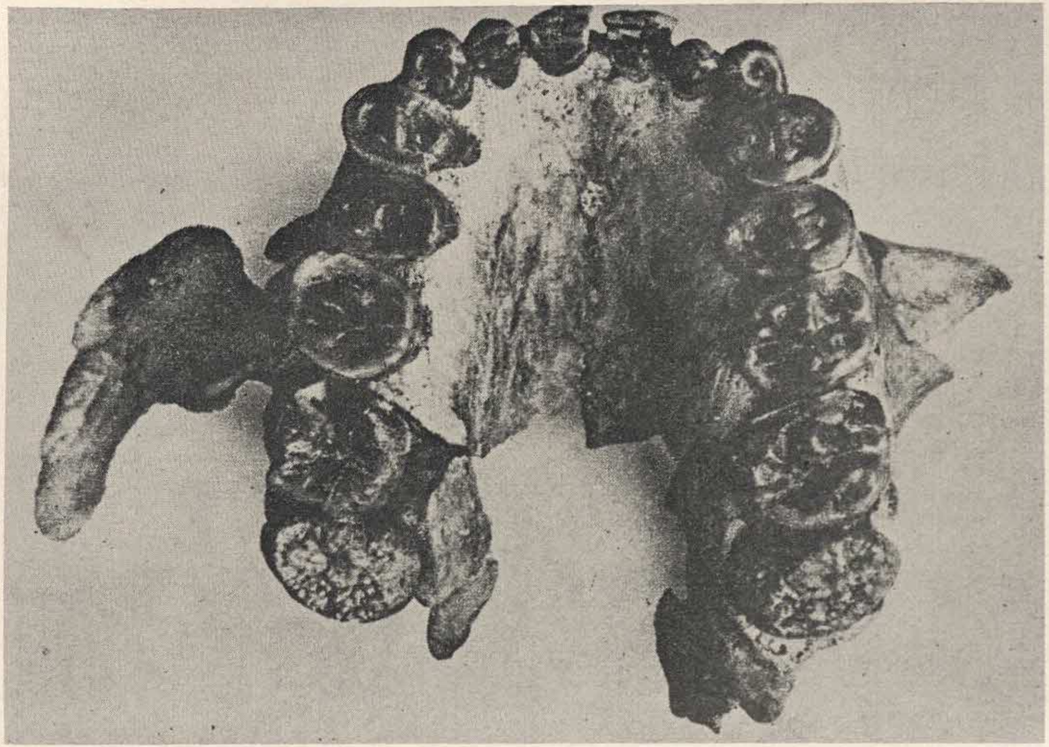

Figure 18. The most recent Australopithecine find was made at Olduvai Gorge, Tanganyika, Africa, in 1959, by Dr. and Mrs. L. S. B. Leakey, and was nicknamed "nutcracker man." The massively developed molar and premolar teeth of the fossil palate contrast with the reduced incisors and canines. While its dentition is hominid, the skull possessed a small sagittal and a pronounced nuchal crest, like that of an ape. Alterations in dentition thus seem leading and primary to further evolutionary modification of the head. Reproduced by permission of United Press International, Inc.

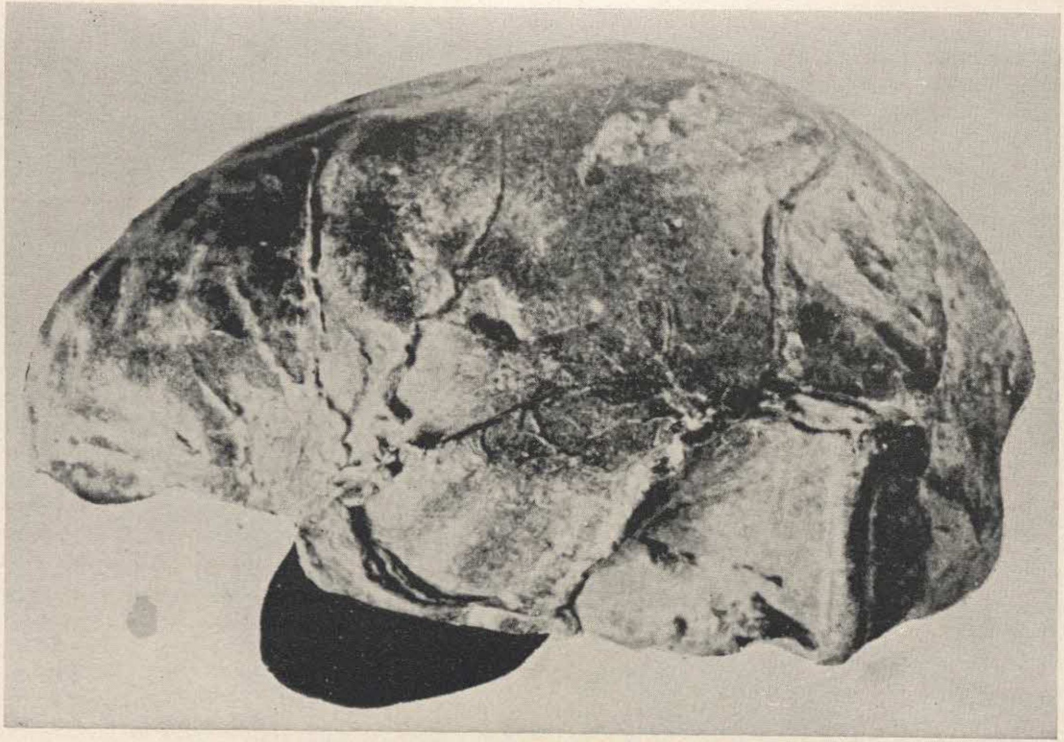

FIGURE 19. The first Australopithecine remains to be discovered contained an almost complete, natural, endocranial cast, the volume of which was exactly 500 cc. (see Figure 14). The prepared cast of "Mrs. Ples," seen here, is even more perfect. The endocranial volume of the African man-apes ranged between 450 and 650 cc. and averaged 550 cc. This is but 100 cc. more than the average volume of the anthropoid brain (450 cc.). Reprinted from Schepers, G. W. H.: The brain casts of the recently discovered *Plesianthropus* skulls. *Transvaal Museum Memoirs*, 4, pt. 2, 1949.

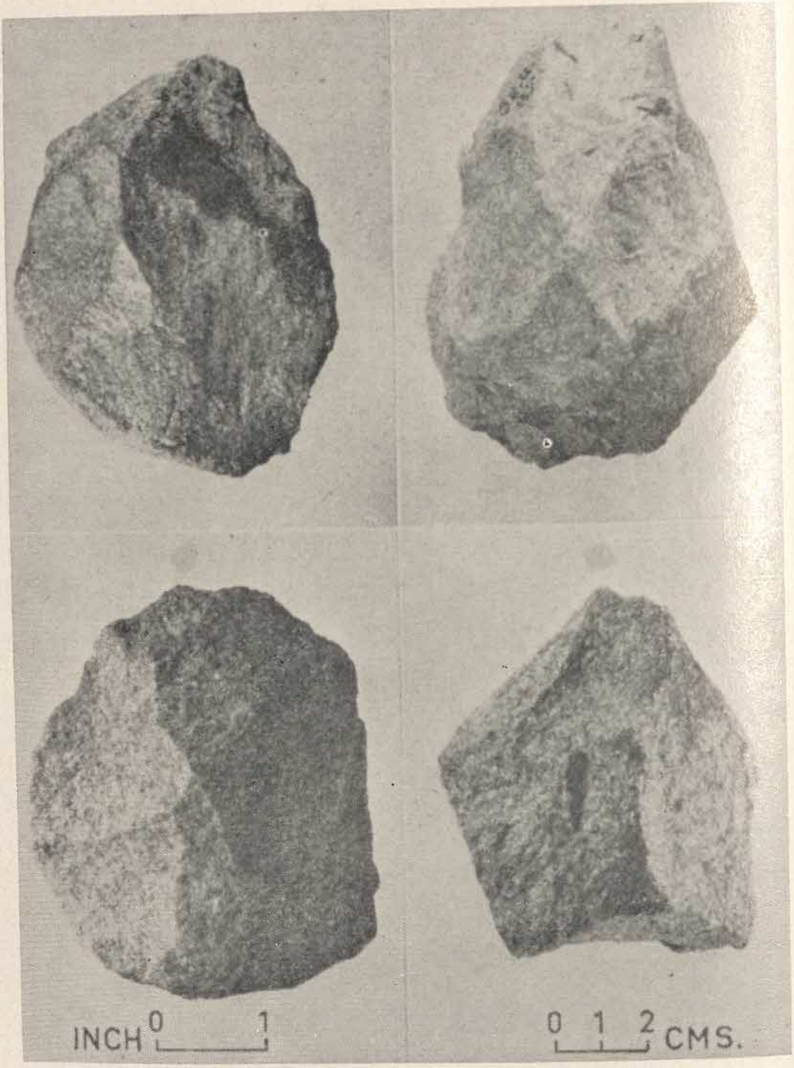

FIGURE 20. The manufacture of tools is sometimes proposed as a distinguishing criterion of man. Pebble tools, made of stone foreign to the cave site, have been recovered with Australopithecine remains. These tools show definite evidence of being trimmed and altered to form hammerstones and choppers. Fragments of horn and bone, also found with Australopithecine remains, suggest the use of natural implements as well. It is additionally likely that all tool-using types employed wooden instruments, but none of such age has been preserved. While these primitive forms were already capable of manufacturing implements, there is so far no clear indication that the Australopithecines had learned to use fire. Reprinted from Robinson, J. T., and Mason, R. J.: Occurrence of stone artifacts with *Australopithecus* at Sterkfontein. *Nature* **18,** *521 (1957)*.

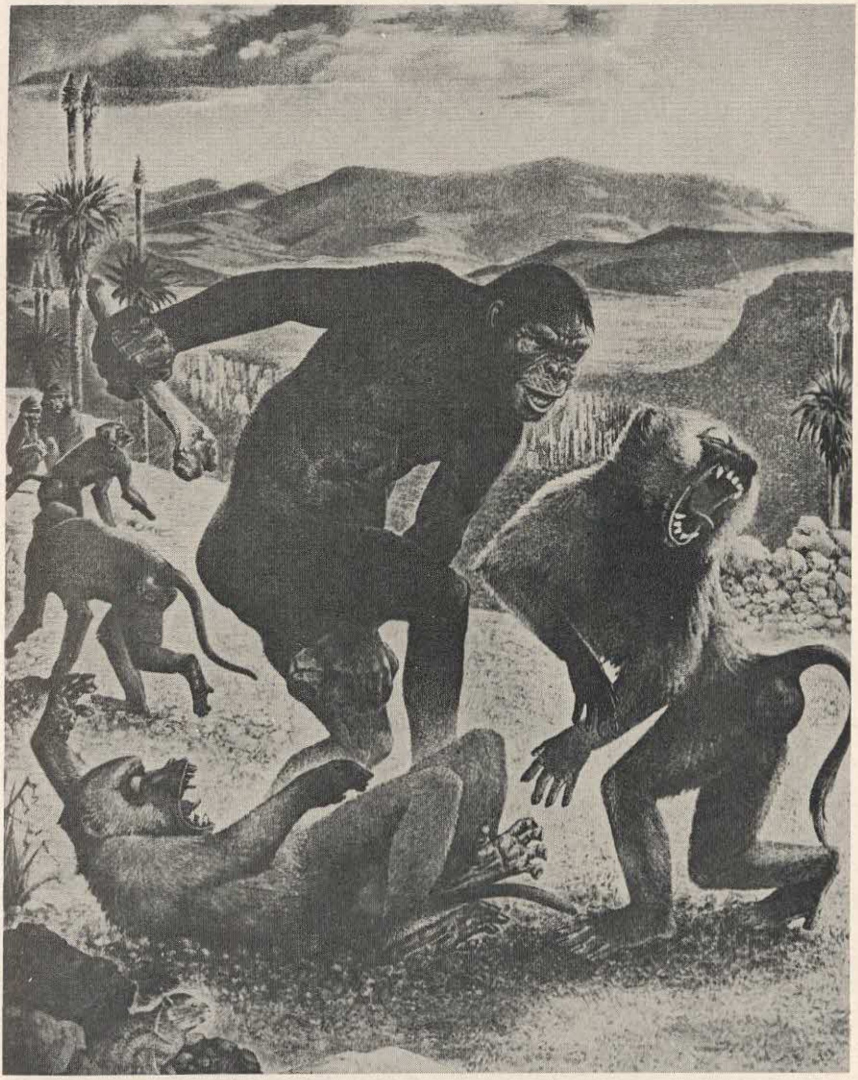

FIGURE 21. In 1946, Dr. Robert Broom wrote: "Man's immediate ancestors were slightly built primates of short stature, who walked or ran on their hind feet. Their hands were mainly used for manipulation of implements." The commonest fossil cave-remains associated with the man-apes were those of extinct baboons. Broom remarked further: "All the baboon skulls I found had depressed fractures on the top of the head. If *Australopithecus* killed the small baboons, we seem forced to believe that he used implements of some sort." This recent painting by Rudolf Freund depicts an erect *Australopithecus* killing baboons with hand-wielded weapons of bone and stone. Reprinted from *Life* 47, *97 (1959)*.

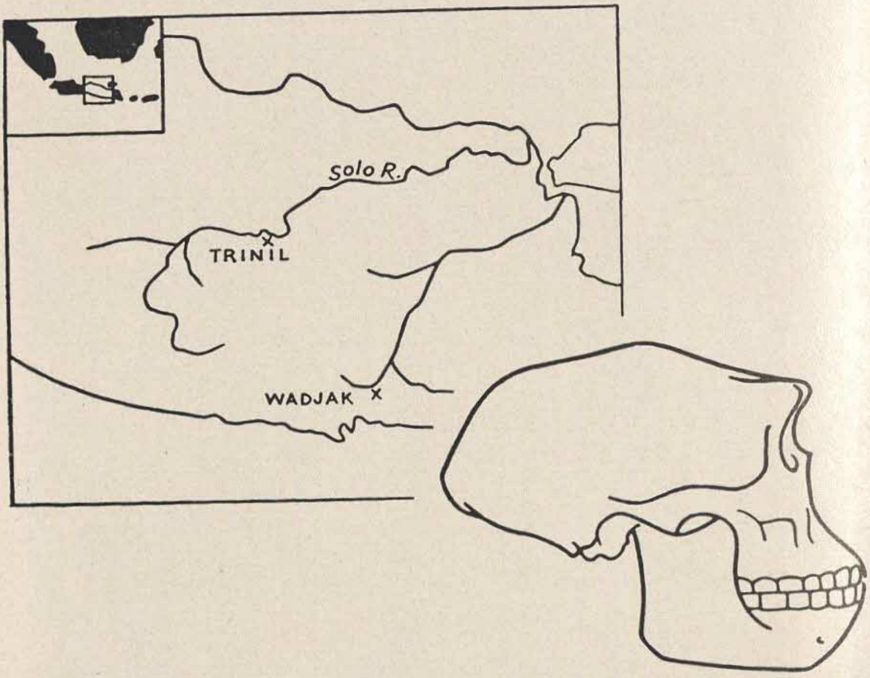

FIGURE 22. In 1890, Eugene Dubois, a physician in the Dutch Colonial Army who was keenly interested in anthropology, discovered a fossil calvarium, femur, jaw, and teeth, in Trinil, Java. He described them as the remains of an "erect-walking ape-man, or a man-like transition form," which became known as the "Ape-man from Java." Dubois' excavations were motivated by Haeckel's views, and his discoveries supported Haeckel's proposal of an Indonesian setting for the evolution of man. Reprinted from Moore, R.: *Man, Time and Fossils.* New York, Knopf, 1953. (Plate drawn by Sue Richard).

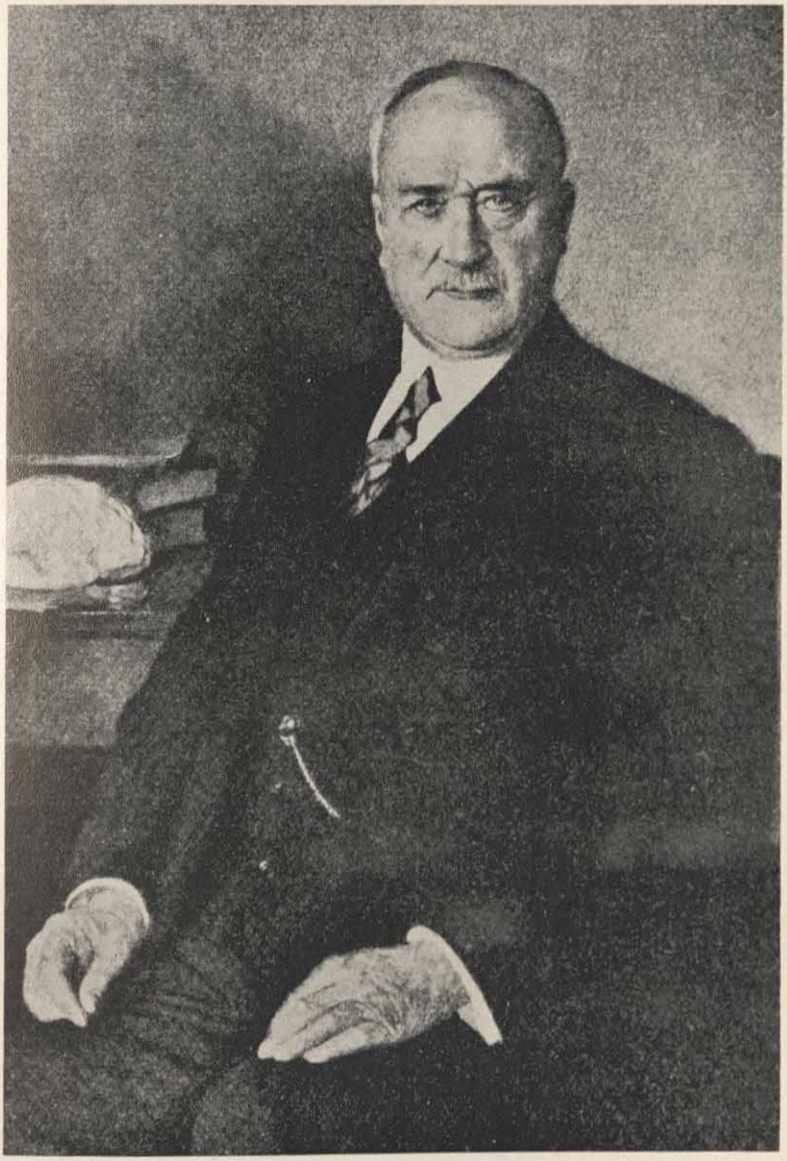

FIGURE 23. On his return from Java, Dubois exhibited his findings at scientific congresses in England and Europe, but became embittered by the opposition they aroused and put the bones away for some 30 years. Although the great value of his discovery was widely recognized before his death in 1940, at the age of 82, his last years were reclusive and he took little interest in his belated triumph. This late photo shows him with an endocranial cast of *Pithecanthropus erectus*.

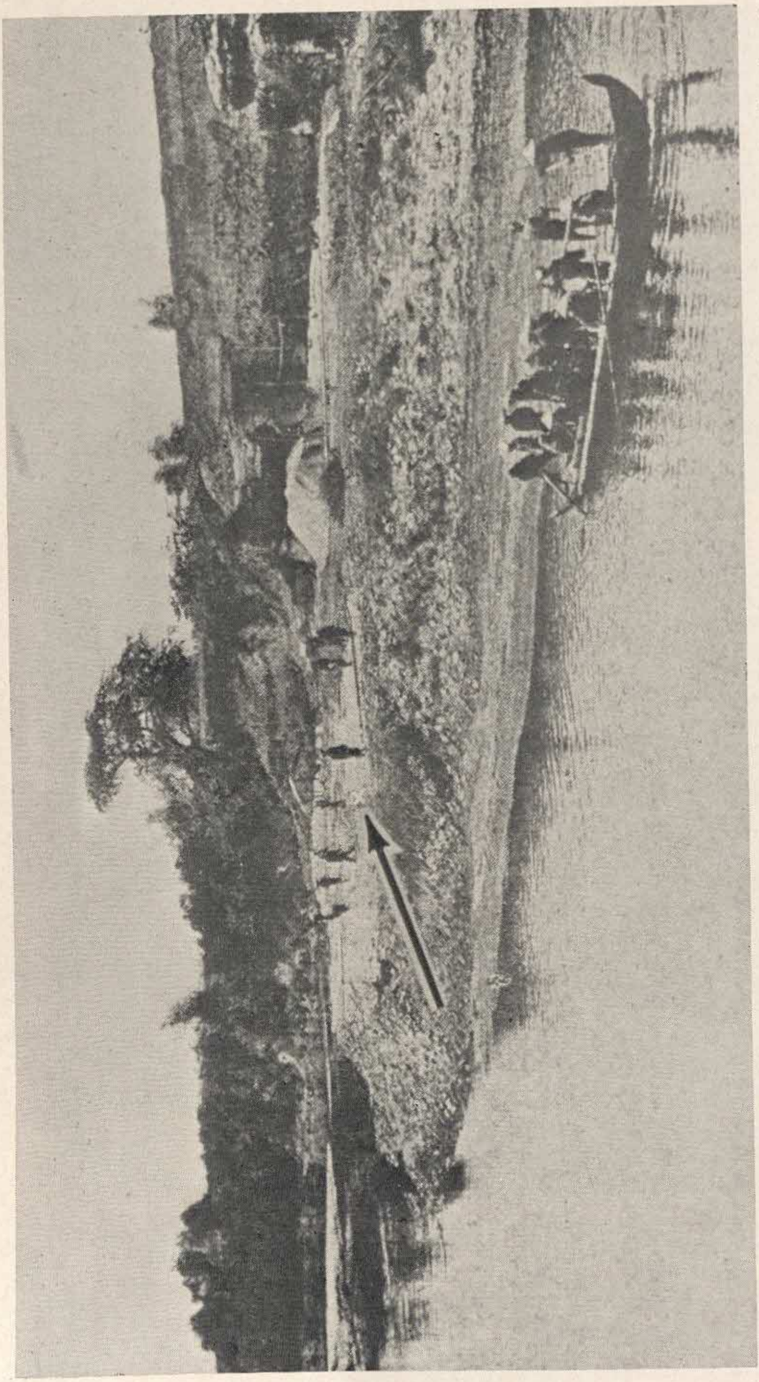

FIGURE 24. This photo of the bank of the Solo River in Trinil, Java, shows (center) the mid-Pleistocene stratum of volcanic tuff from which Dubois excavated Java man. Much later, Dubois' work was continued in Java by the talented young Danish anthropologist, G. H. R. von Koenigswald, who found additional Pithecanthropoid remains on the weathered slope of a river-bed at Sangiran.

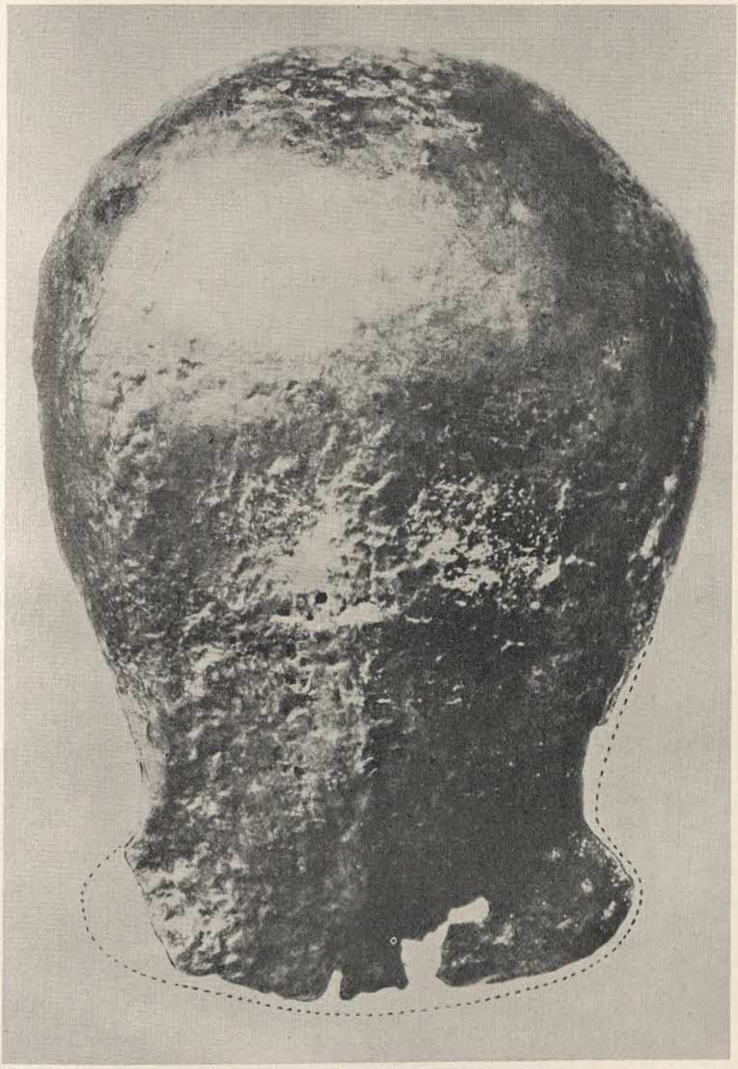

FIGURE 25. The famous skull-cap of Java man, from Trinil, possessed massive brow-ridges and a forehead the slope of which was so low as to imply a limited development of the underlying brain. The femur was essentially like that of a modern man, however, and unquestionably indicated an erect posture. Like the Australopithecines before him, Java man thus possessed an admixture of simian and hominid features, characteristic of an intermediate evolutionary type. His cranial capacity, however, was considerably larger than the African man-ape's. Reprinted from Dubois, E.: *Pithecanthropus erectus; eine menschenaehnliche Ubergangsform aus Java.* Batavia, 1894.

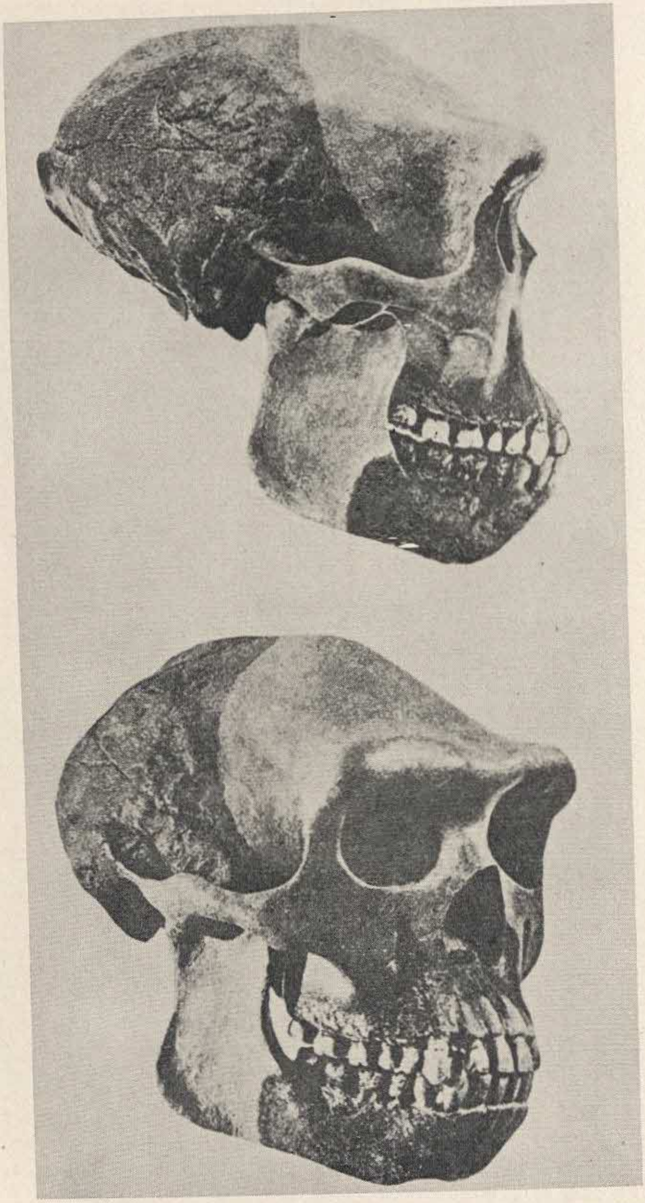

FIGURE 26. A reconstruction of the skull and jaw of Java man, prepared by Franz Weidenreich, chiefly from the Sangiran remains, further emphasized his intermediate stage of development. The low forehead, beetling brow, and massive jaw are all conspicuous features. The jaw even possessed a simian gap in dentition, to accommodate the canine teeth during occlusion. Reprinted from Weidenreich, F.: *Apes, Giants and Men*. Chicago, University of Chicago Press, 1946.

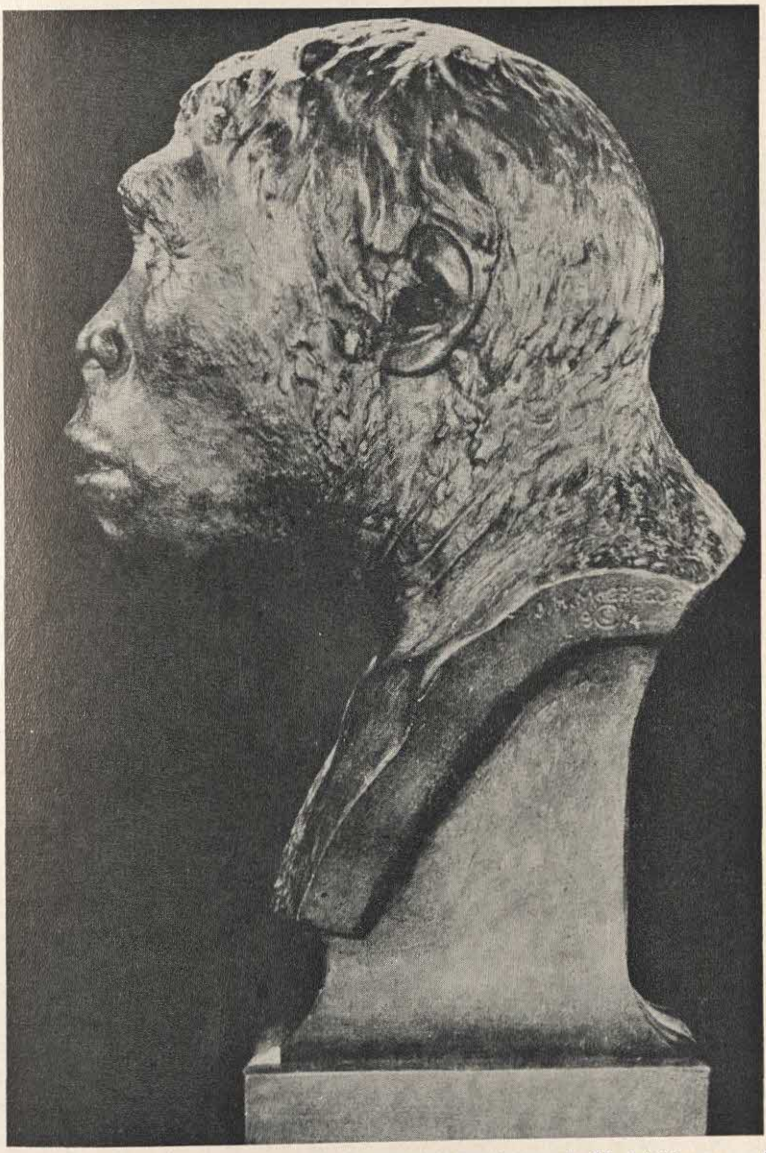

FIGURE 27. A reconstruction of Java man by Professor J. H. McGregor of the American Museum of Natural History, New York, emphasized the transitional stage between ape and man. Because all of the Java remains were recovered in a fragmented state, from exposed positions in river banks or hillsides, it has not been possible to obtain associated cultural remains. In this respect, as in others, the more recent discoveries of Peking man have greatly extended our knowledge of the Pithecanthropoids.

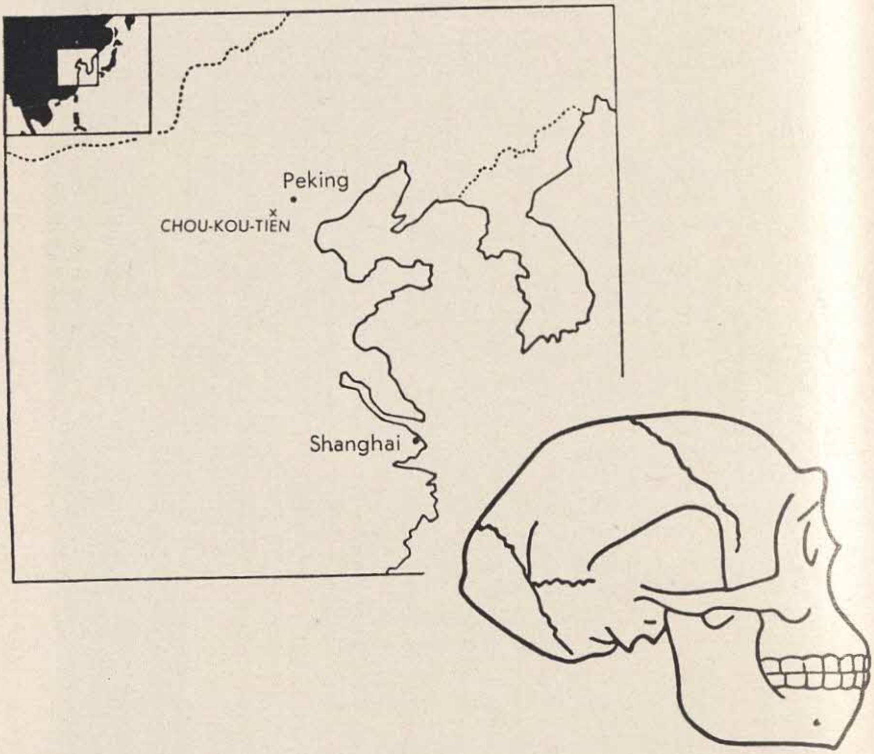

FIGURE 28. In 1926, a lower molar, hominid tooth was recovered from the hillside, from a middle Pleistocene layer, in the limestone quarry at Chou-Kou-Tien, near Peking, China. The existence of Peking man was proposed, on the basis of this single tooth. In the years following, up to World War II, remains of some forty individuals were obtained, providing a wealth of support for Dubois' earlier contested findings in Java. Java and Peking man are now considered the type-hominids of the mid-Pleistocene period and, as Dubois originally proposed, they truly constitute a transition form to modern man. Reprinted from Moore, R.: *Man, Time and Fossils*. New York, Knopf, 1953. (Plate drawn by Sue Richard).

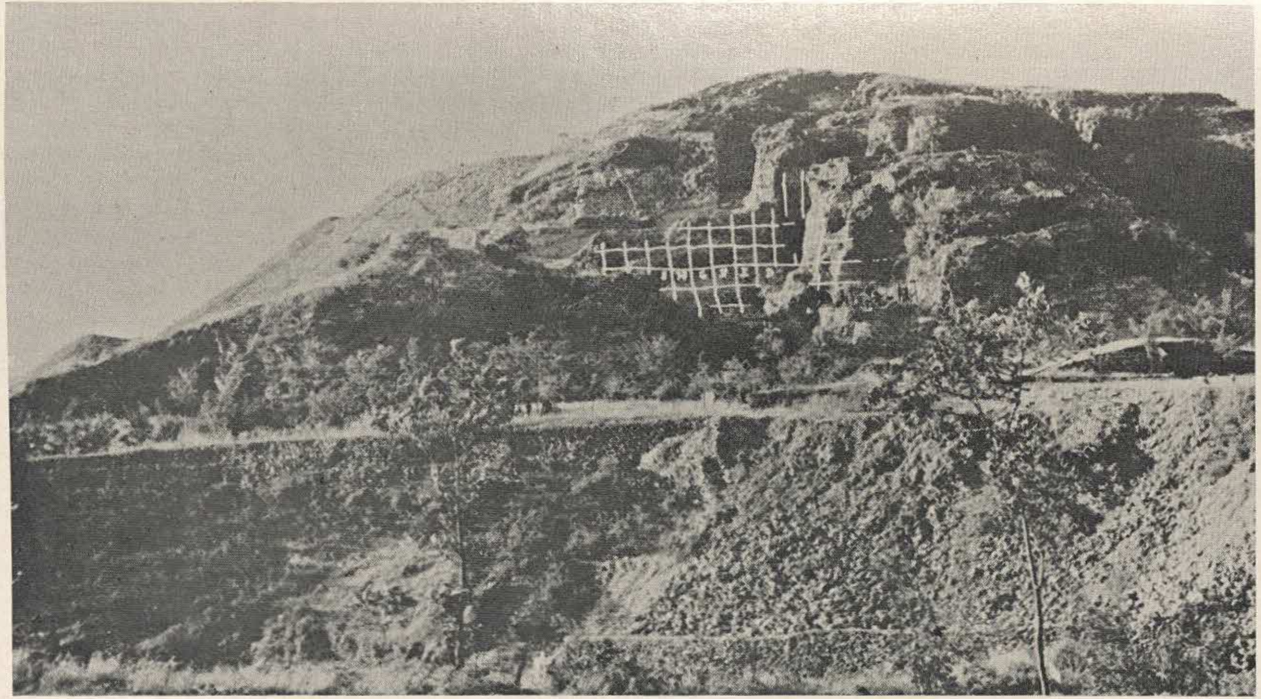

FIGURE 29. With support from the Rockefeller Foundation, one of the most elaborate programs of anthropological excavation ever to be undertaken was begun at Chou-Kou-Tien. A numbered grid was marked out on the side of the hill and, in systematic digging, the prehistoric contents of the caves of Dragon Mountain were recovered. The work, which was directed by the young Chinese archaeologist, C. Pei, produced a rich collection of skeletal remains of Peking man, together with his stone implements and evidence of his use of fire.

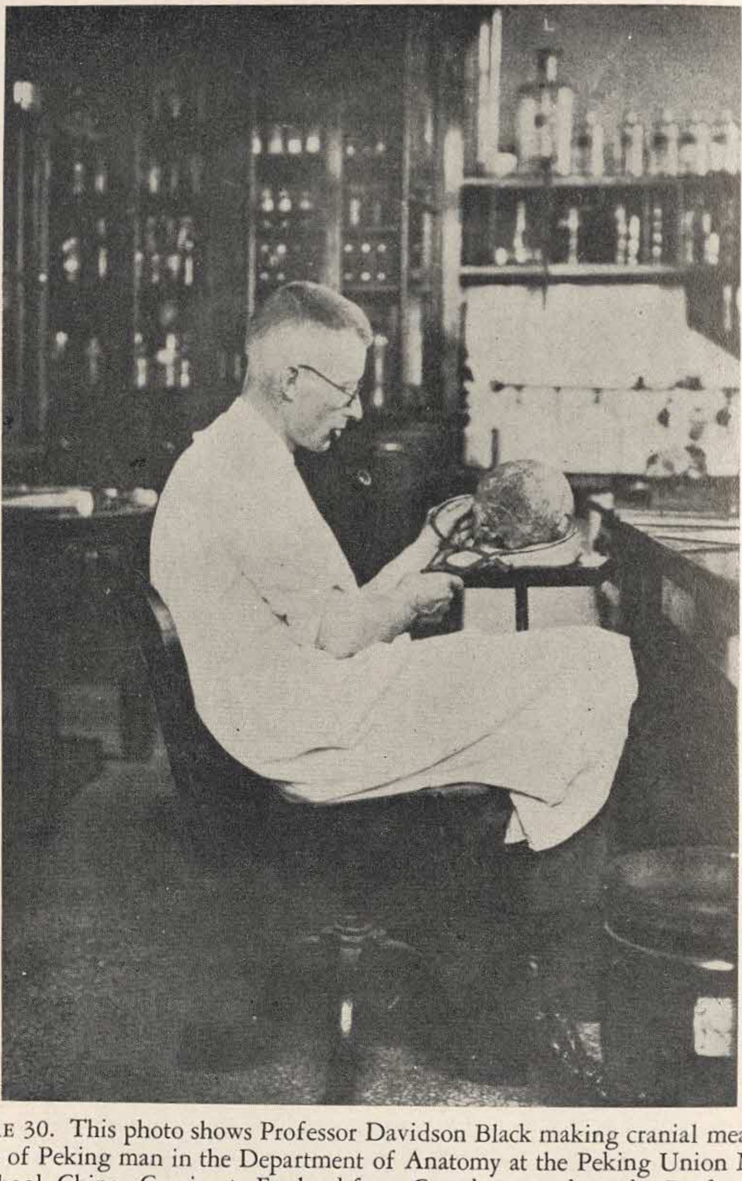

FIGURE 30. This photo shows Professor Davidson Black making cranial measurements of Peking man in the Department of Anatomy at the Peking Union Medical School, China. Coming to England from Canada, to study under Professor G. Elliot Smith, Black was fascinated by the research then under way on the Piltdown skull and determined to make anthropology his life work. Convinced that China was the place where primitive man was likely to be discovered, he accepted an appointment in Peking. Following the initial find, he kept the famous fossil tooth in a little brass case, attached to his watch chain, and toured the world to enlist support for further work.

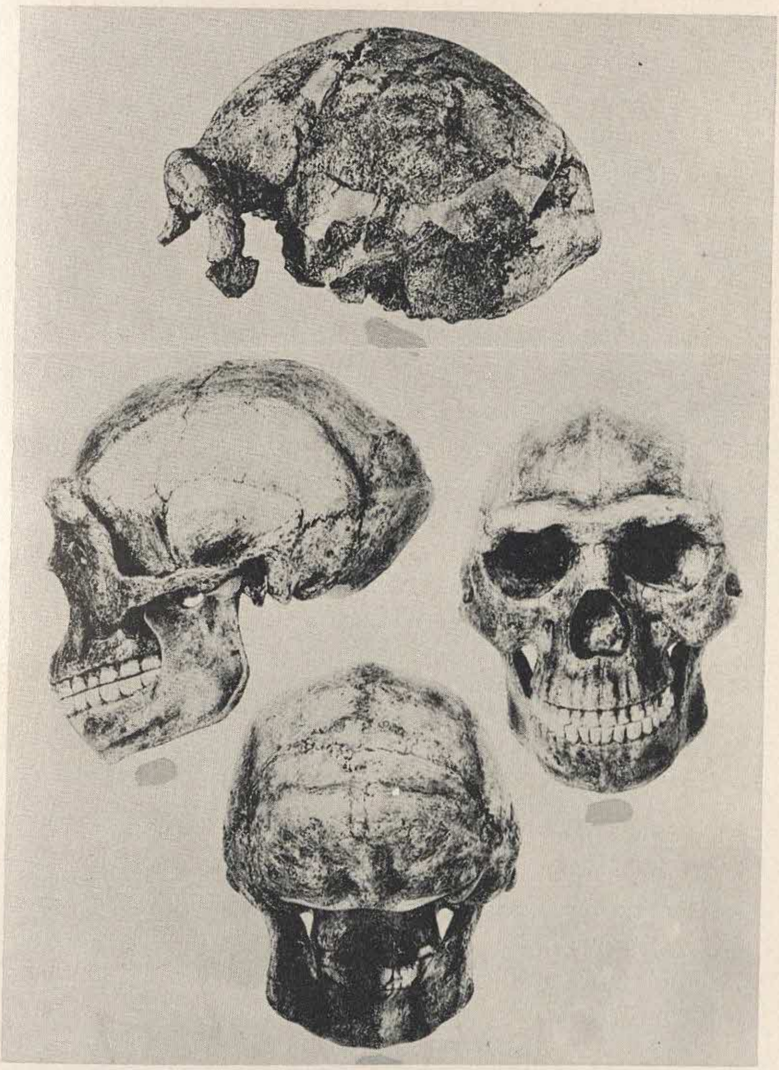

FIGURE 31. The suggestion has been made that Peking man was a cannibal. Human thigh bones, scattered throughout the deposits, appeared to have been split open for marrow, as were the bones of other animals known to have been eaten for food. Some of the skulls showed signs of heavy blows, and others appeared to have been "opened from the base, probably for the purpose of reaching their contents, namely the brains." Reconstruction of the skull of Peking man were prepared by Franz Weidenreich, who continued their study following the death of Davidson Black in 1934. Reprinted from Weidenreich, F.: The skull of *Sinanthropus pekinensis*: a comparative study on a primitive hominid skull. *Paleontologia sinica* n.s. D, 10 *(1943)*.

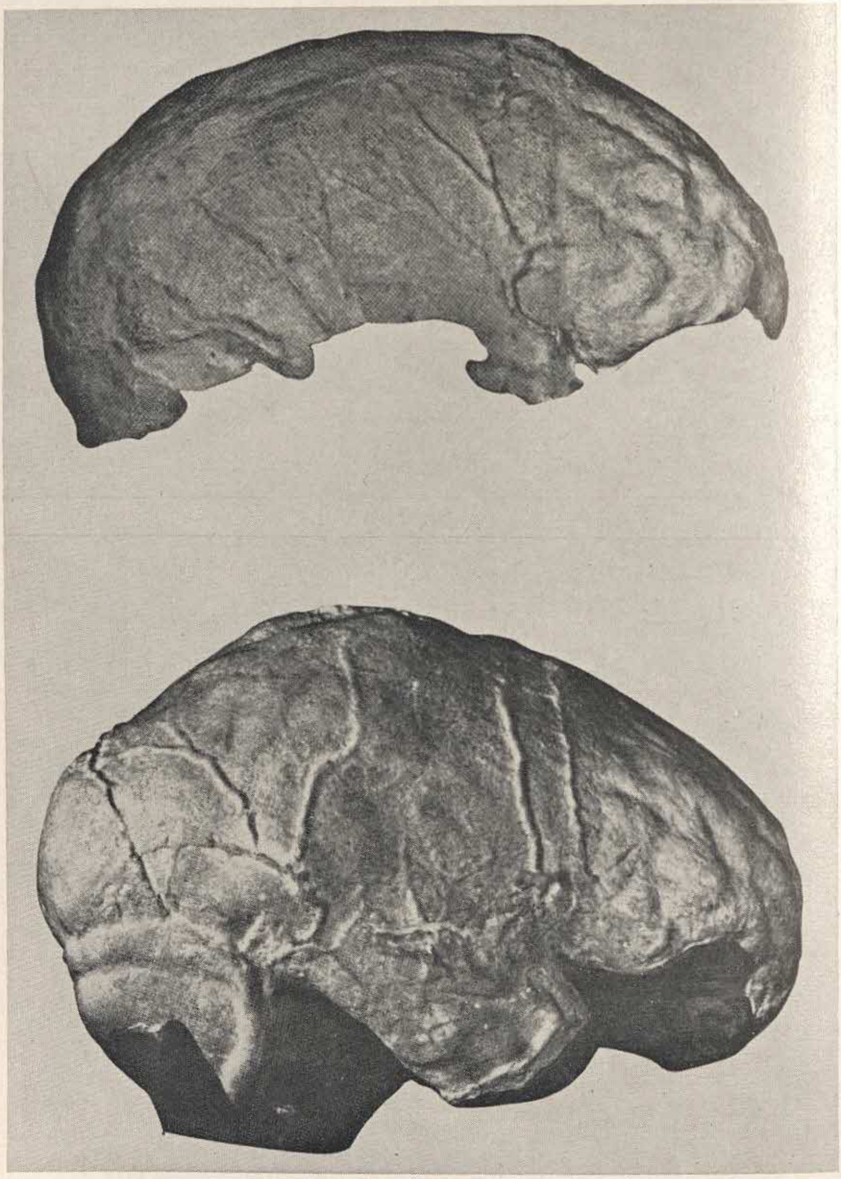

FIGURE 32. Endocranial casts of Java man (above) and Peking man (below) indicate the close similarity of their brains. In the cast of the Java man, shown here in lateral view, the sculpturing of the frontal convolutions of the brain is quite remarkable. Reprinted from Dubois, E.: The shape and size of the brain in *Sinanthropus* and *Pithecanthropus. Proc. Sect. Sc. K. Akad. Wetensch., Amsterdam* 36 *(Part 1), 415 (1933).*

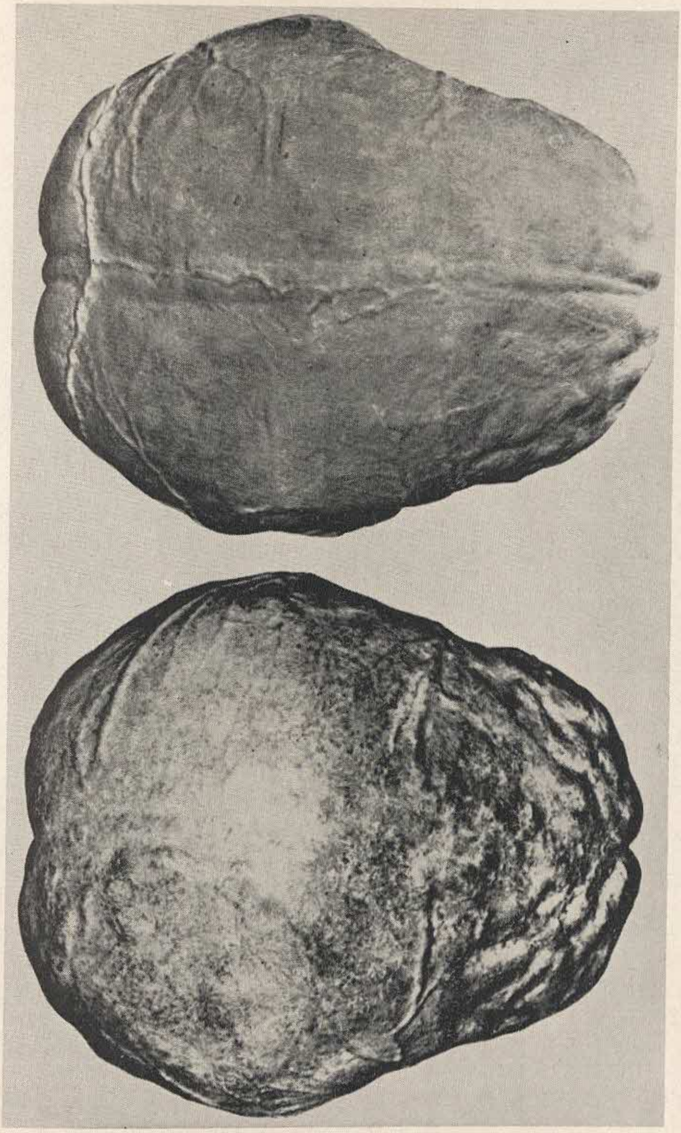

FIGURE 33. The endocranial casts of Java man (above) and Peking man (below), shown here in dorsal view, indicate the close similarity of their brains. The cranial capacity of Java man averaged 850 cc. (range, 750 to 900 cc.); while that of Peking man was somewhat greater, averaging 1050 cc. (range, 900 to 1200 cc.). Reprinted from Dubois, E.: The shape and size of the brain in *Sinanthropus* and *Pithecanthropus. Proc. Sect. Sc. K. Akad. Wetensch., Amsterdam* 36 *(Part 1), 415 (1933).*

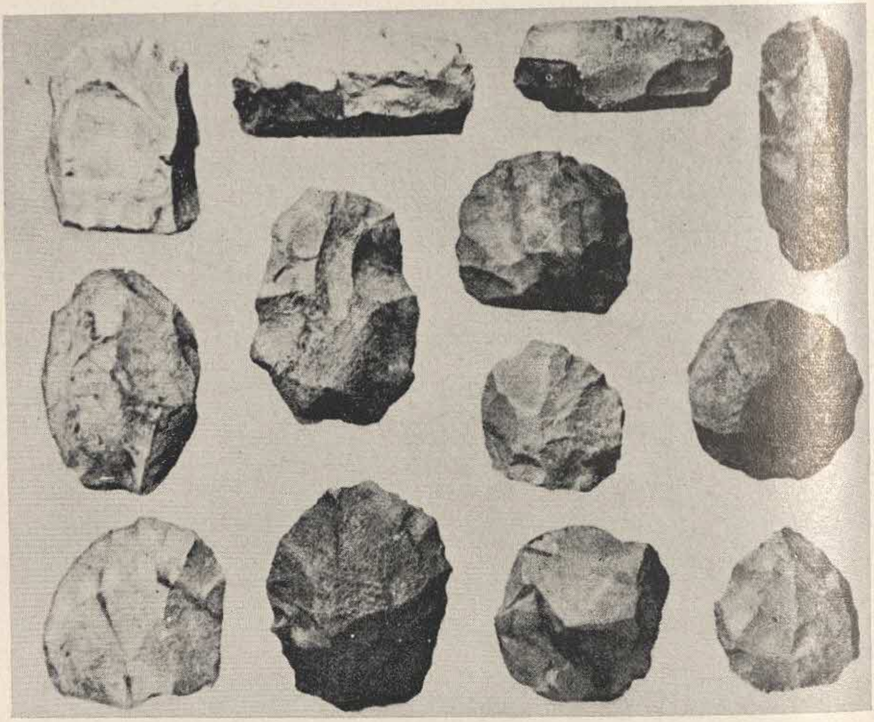

FIGURE 34. In the limestone caves of Chou-Kou-Tien, Peking man manufactured chopper tools and used fire. Many remains were found of the animals he hunted, chief of which was the antelope. His stone implements were somewhat more elaborately prepared than the pebble tools of the Australopithecines but were crude by comparison with later developments. It was Davidson Black's impression that some of these stone implements were fashioned so as to favor use by the right hand. Reprinted from Black, D., *et al.*: Fossil man in China. *Men. Geol. Surv. China*, ser. A., no. 11, 1933.

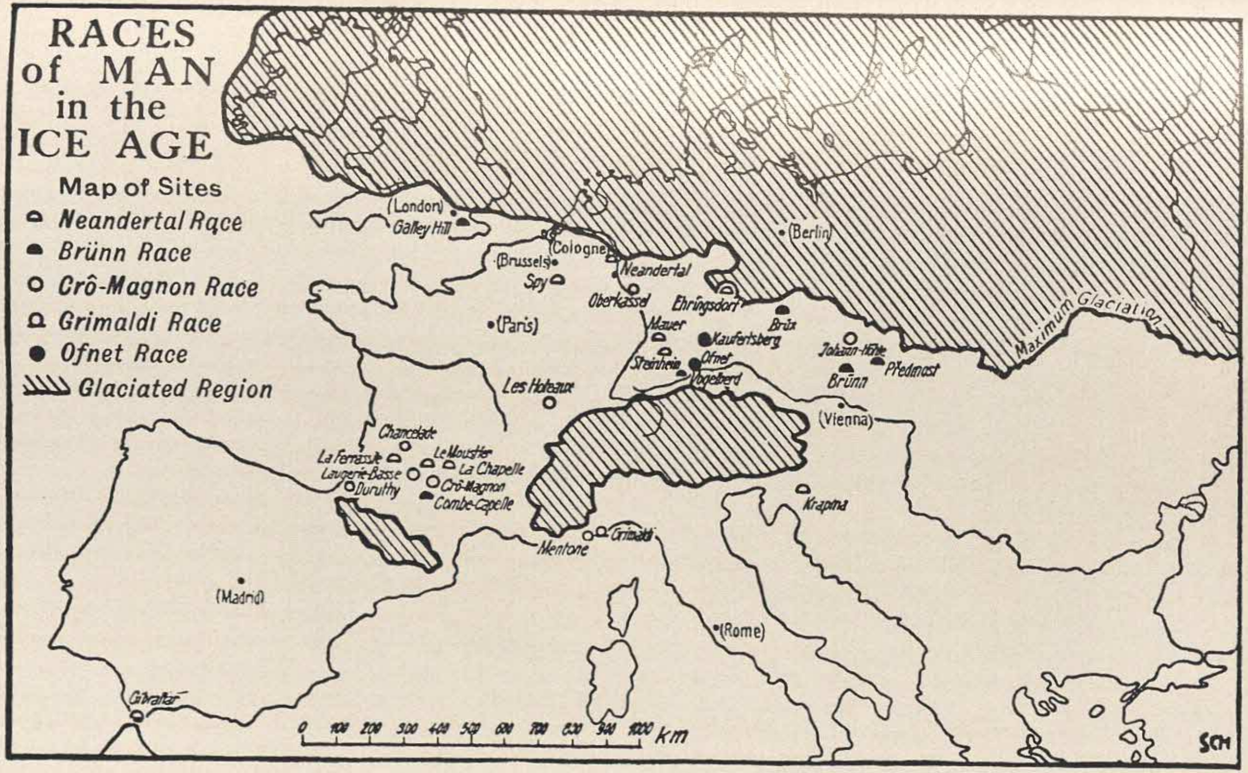

FIGURE 35. On this map, symbols mark the sites at which remains of Upper Pleistocene man have been discovered in Europe. Their distribution is in two zones, parallel to the front of glaciation, the greatest extent of which is marked by shading. The first zone extends across Southern England and Germany into Czechoslovakia, and includes the site of discovery of the original Neanderthal remains. A second, more southern, zone extends across lower France. In this French setting are located the sites of Le Moustier and La Chapelle aux Saints, each yielding important discoveries. Reprinted from Schmidt, R. R.: *The Dawn of the Human Mind*. London, Sidgwick and Jackson, 1936.

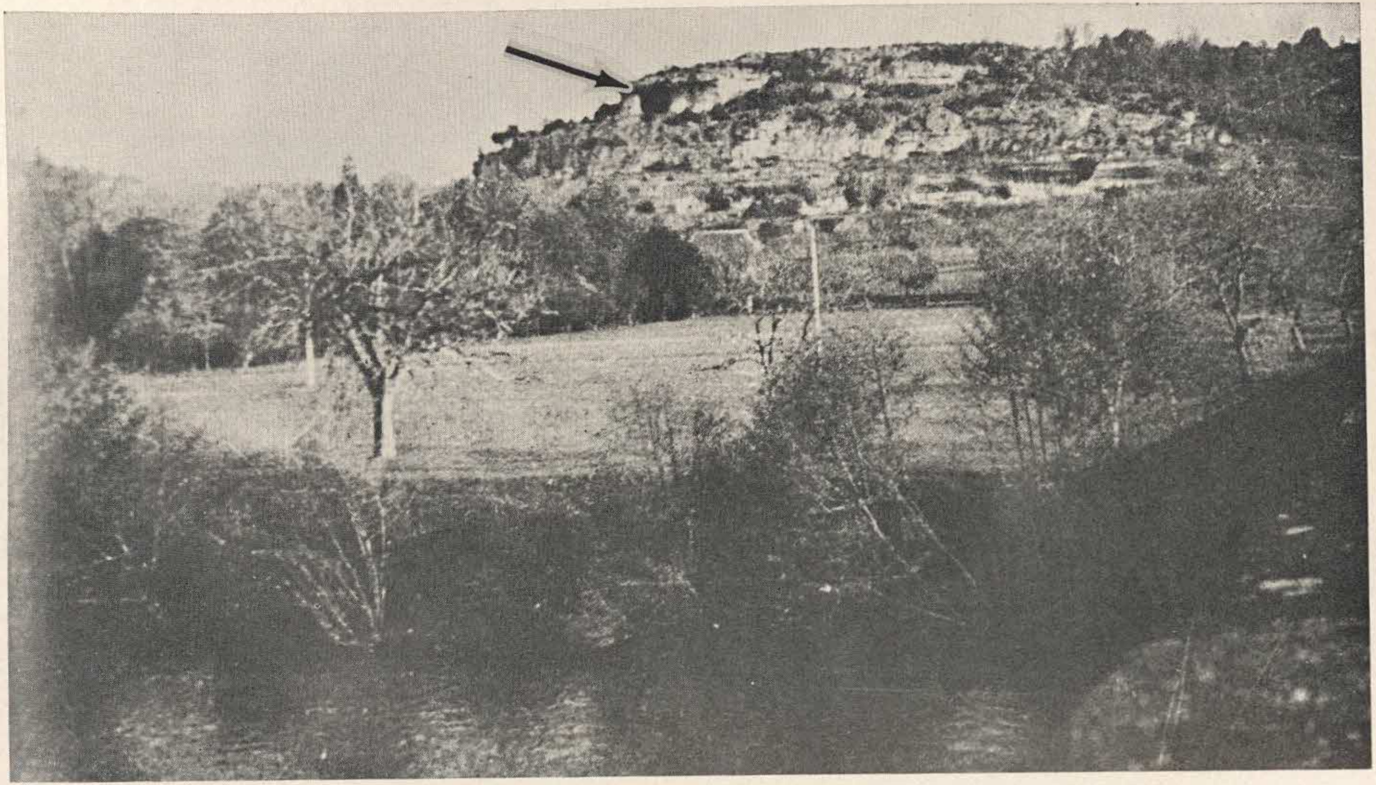

FIGURE 36. As in the earlier case of the Australopithecines, and Peking man, sites where prehistoric man occupied caves have provided the richest collection of anthropological material. In Europe, both Neanderthal and, later, Cro-Magnon man similarly inhabited caves. That in the upper center, overlooking Le Moustier River in Southern France, yielded the most perfectly preserved skeleton of Neanderthal man. Purchased by Germany for the Kaiser Friedrich Museum in Berlin, it was destroyed by bombing in World War II.

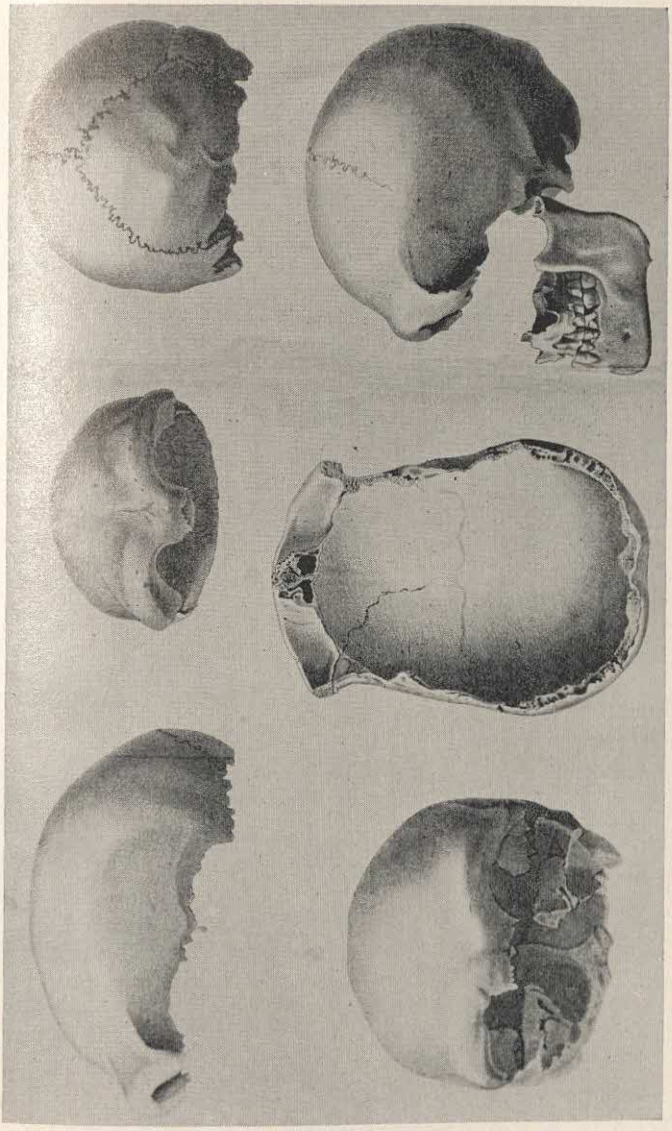

FIGURE 37. The first recognized remains of Neanderthal man were found by Dr. J. K. Fuhlrott in a cave in the Neander Gorge, near Düsseldorf, in Southern Germany in 1856. They were described by Professor H. Schaafhausen, anatomist at Bonn, in a paper entitled "On the Crania of the Most Ancient Races of Man." These bones, Professor Schaafhausen concluded, "may be regarded as the most ancient memorial of the early inhabitants of Europe," a view strenuously opposed by Virchow. The centenary of the discovery of Neanderthal man was celebrated in 1956 at scientific meetings both in Leiden and in New York. The original figures of the Neanderthal skull are here reprinted from Schaafhausen, H.: Zur Kenntniss der altesten Rassenschadel. *Arch. Anat. Physiol.* s. 453 *(1858).*

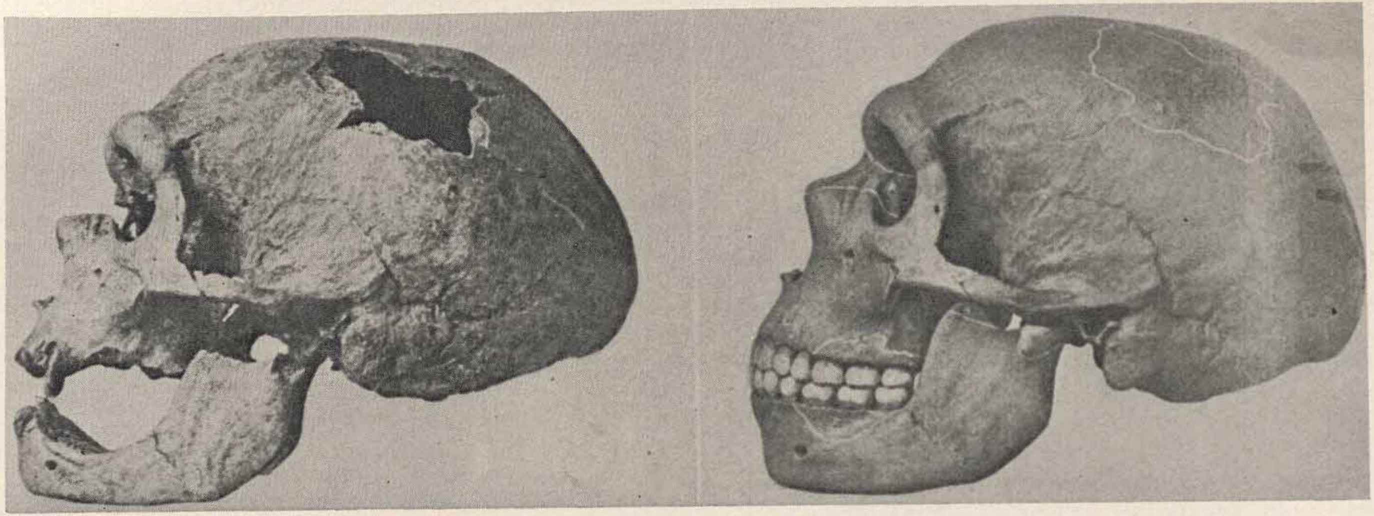

FIGURE 38. Discovery of Upper Pleistocene man in Southern France provided a great stimulus to French anthropology. In particular, knowledge of Neanderthal man was advanced by M. Boule, through study of the "Old Man" discovered in a shallow grave at La Chapelle aux Saints. It is now proposed that this individual may have been no older than 40 years. Neglect of oral hygiene resulted in the carious loss of most of his teeth. Deforming spinal arthritis was responsible for the stooped posture in which he was reconstructed. While his brow ridges and jaw were conspicuous, present interpretations favor, rather than oppose, his affinity to modern man. Reprinted from Boule, M., and Vallois, H. V.: *Fossil Men.* New York, Dryden Press, 1957.

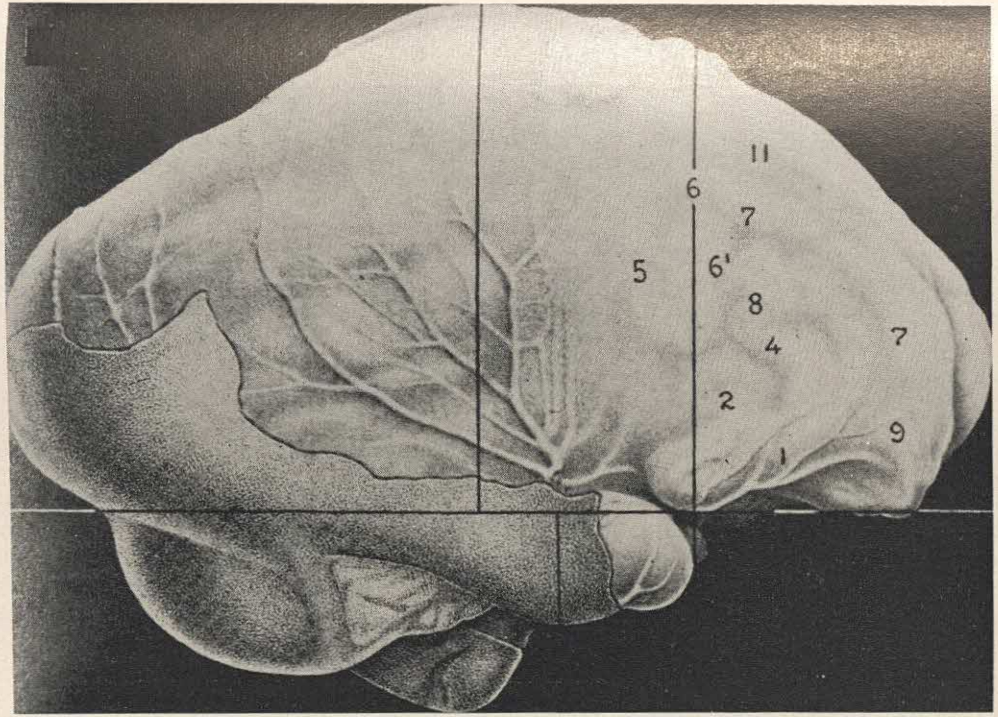

FIGURE 39. Most remarkable of all, the brain of Neanderthal man, seen here in reconstruction by C. U. Ariens Kappers, seems already to have gained the dimensions of contemporary man's brain. The cranial capacity of the "Old Man of La Chapelle aux Saints" was estimated at 1620 cc. Other specimens range between 1300 and 1450 cc., with an average of 1360 cc. If one follows the increment in the size of the brain, from 550 cc. in the Australopithecines, to 1000 cc. in the Pithecanthropoids, to 1360 cc. in Neanderthal man, the last would appear to be just short of modern man, whose average is usually given as 1450 cc. Reprinted from Ariens Kappers, C. U.: Further communication on the fissures of the frontal lobes in Neanderthal men. *Proc. Sect. Sci. K. Akad. Wetensch., Amsterdam* 32 *(Part 1), 196 (1929).*

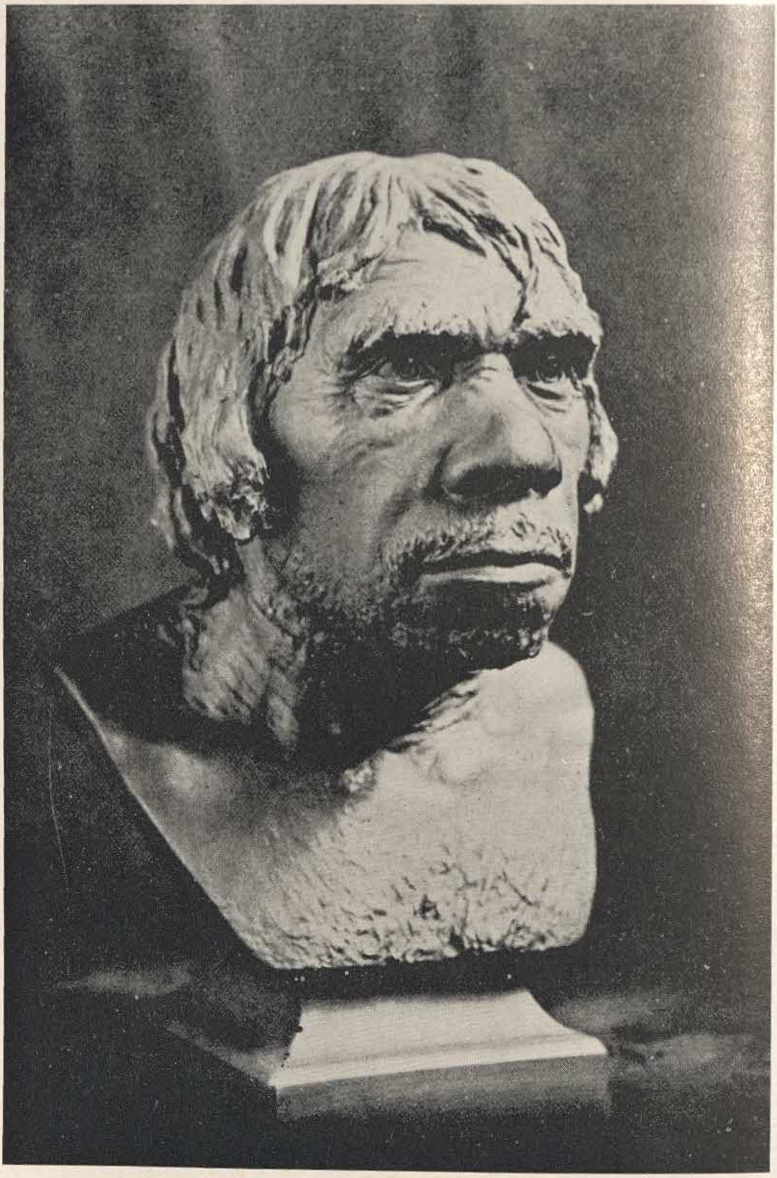

FIGURE 40. This reconstruction of Neanderthal man, by Professor J. H. McGregor, of the American Museum of Natural History, New York, stresses the previously emphasized simian characteristics. Taking his cerebral expansion into account, the limitations of Neanderthal man's cultural development seem to form a much more interesting question, today, than the presumed simian features of his appearance.

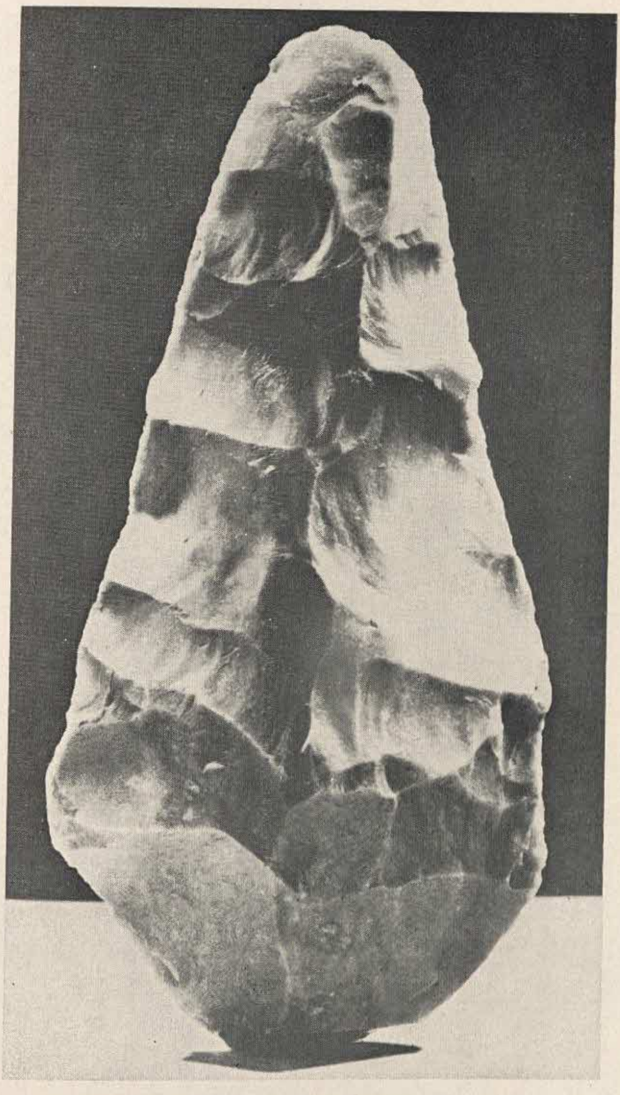

FIGURE 41. A progressive advance in manufacture of tools can be traced from the crude pebble tools of the Australopithecines, through the somewhat more elaborate chopper implements of the Pithecanthropoids, to the flint points, cores, and hand axes of Neanderthal man. Neanderthal implements were prepared from special types of flint, displayed some diversity and specialization, and were executed with a degree of craftsmanship lacking at earlier stages. It would thus seem possible to trace a cultural parallel to the gradual increment of the brain in hominid evolution. Reprinted from Coon, C. S.: *The Story of Man*. New York, Knopf, 1955.

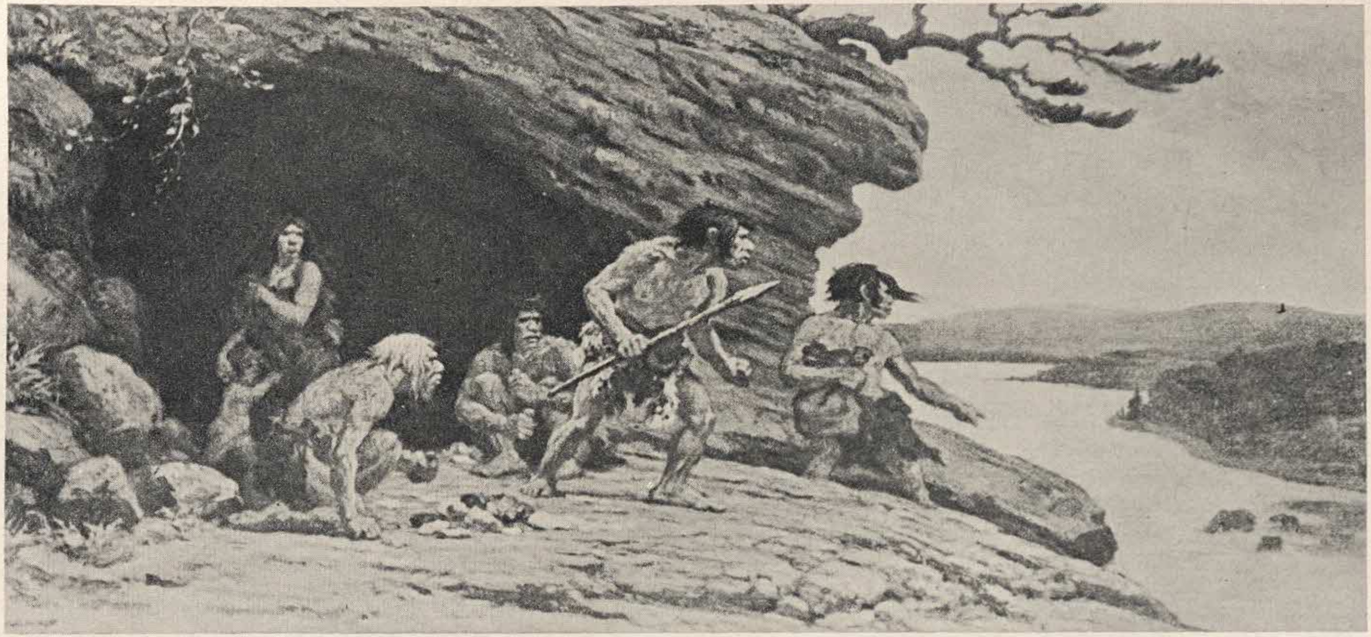

FIGURE 42. This painting by Charles R. Knight, of the American Museum of Natural History, New York, shows a family of Neanderthal flint workers at the mouth of the cave at Le Moustier overlooking the Vézère Valley in Southern France (see Figure 36). Among the features depicted are: family and child-rearing relations; the use of animal skins for clothing; and the gathering of flint stones (right) and their manufacture into implements by the two squatting figures. The attention of the group has been attracted to the presence of rhinoceros in the river-bed, and a hunt with stone-pointed spears seems about to begin.

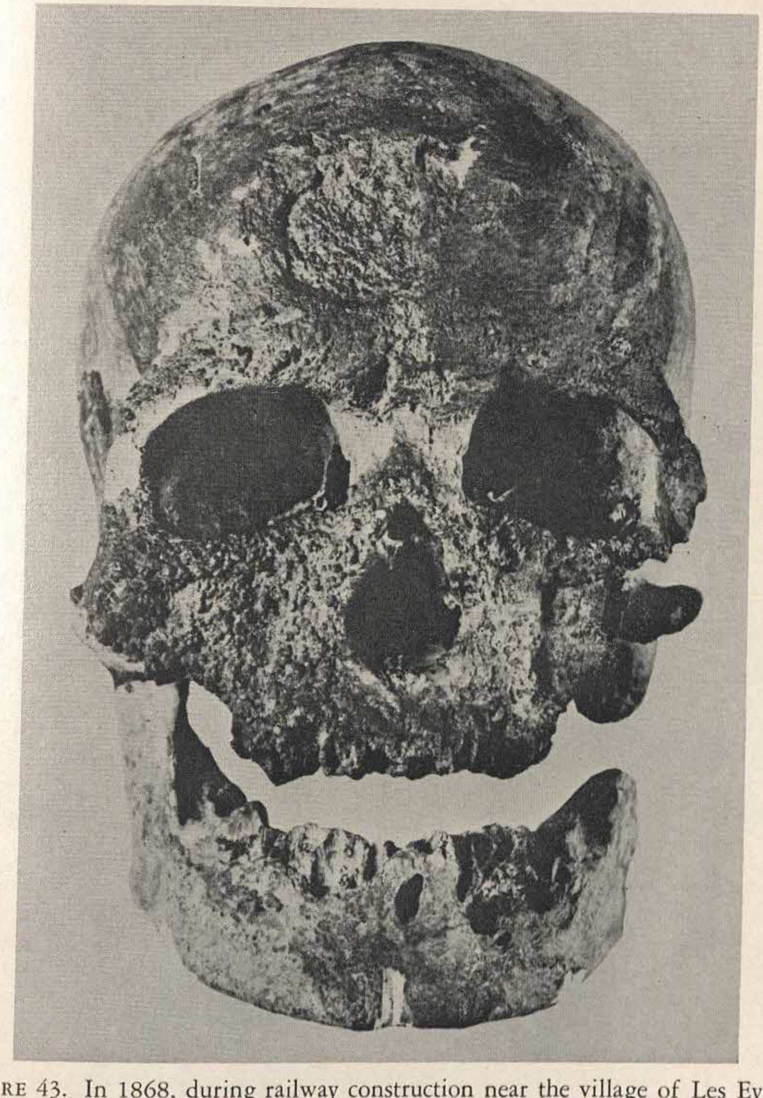

FIGURE 43. In 1868, during railway construction near the village of Les Eyzies in Southern France, the Cro-Magnon cave was discovered. In it were found remains of weapons, tools, ornaments, game, and five human skeletons, including "the Old Man of Cro-Magnon." His striking skull, seen here, with high forehead, broad face, and prominent nose and chin, became the type specimen of Cro-Magnon man, the earliest representative of *Homo sapiens*, living 25,000 to 50,000 years ago. His range of European habitation was much the same as Neanderthal man's and is marked with open circles in Figure 35. Reprinted from Broca, P.: Sur les crânes et ossements des Eyzies. *Bull. Soc. Anthrop., Paris.* Ser. 2, 3: *350 (1868).*

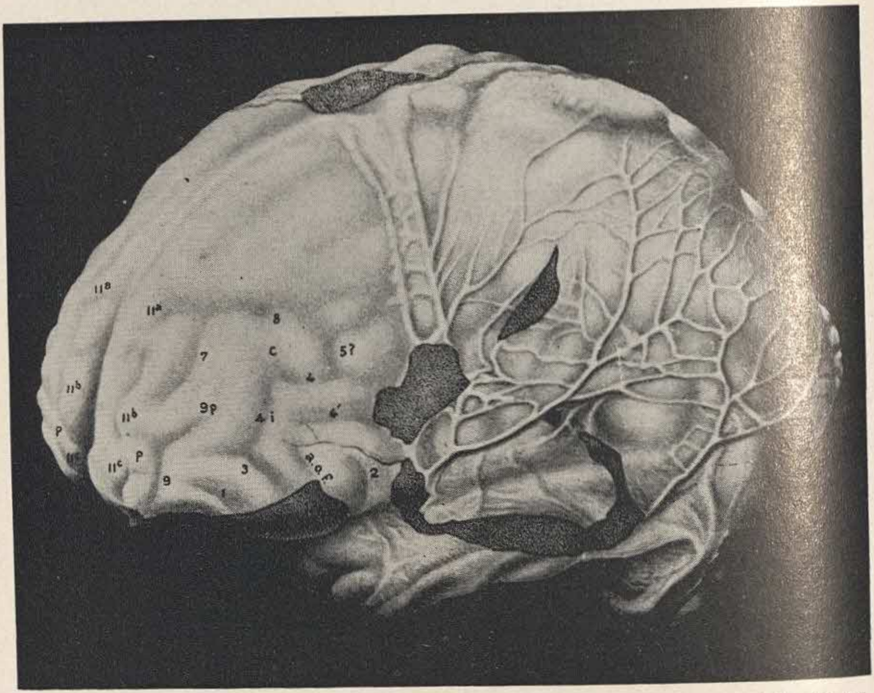

FIGURE 44. An endocranial cast of Cro-Magnon type man, prepared by C. U. Ariens Kappers from the Predmost Skulls of Moravia, shows an essentially modern brain. Cranial capacities of these skulls range from 1308 to 1568 cc., and average 1435 cc. The capacities of other specimens are: 1415 cc. (Combe-Capelle); 1590 cc. (Cro-Magnon); and 1530 cc. (Chancelade). An over-all average of 1475 cc. is sometimes given, equivalent to and possibly slightly larger than that of modern man (1450 cc.). With Cro-Magnon man, the development of the brain in hominid evolution was complete. Reprinted from Ariens Kappers, C. U.: The fissures on the frontal lobes of *Pithecanthropus erectus* compared with those of Neanderthal men, Homo recens and chimpanzee. *Proc. Sect. Sci. K. Akad. Wetensch., Amsterdam*, 32 *(Part 1), 182 (1929).*

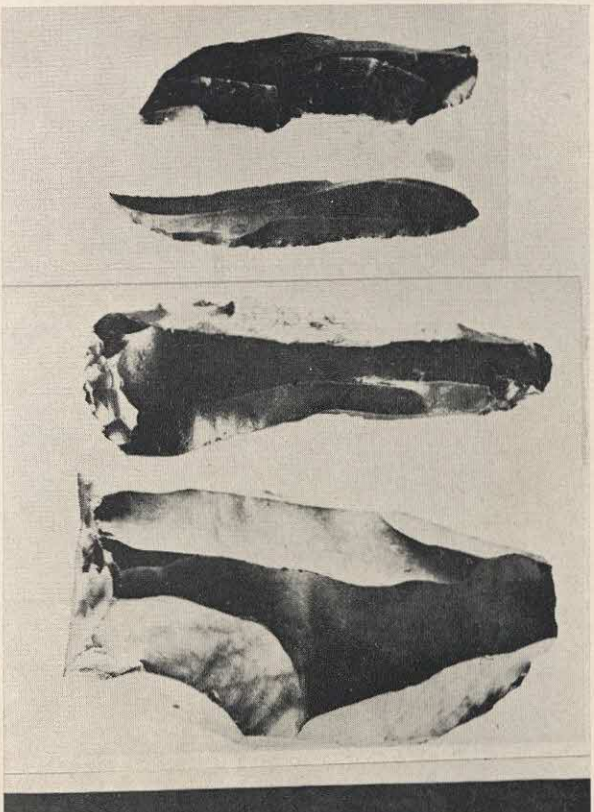

FIGURE 45. Cro-Magnon man has often been called "the Paleolithic Greek" for his many cultural accomplishments. He was primarily a hunter, however, stalking game with spear and later with bow and arrow, for both of which he fashioned points of flint. Additionally, he was a fisherman, making hooks and harpoons from bone. He also perforated bone for needles and is presumed to have sewn animal skins together for clothing. Though fossil *Homo sapiens* continued to employ only flint and bone material, the variety and excellence of his tools and weapons far excelled those of his predecessors. Reprinted from Coon, C. S.: *The Story of Man*. New York, Knopf, 1955.

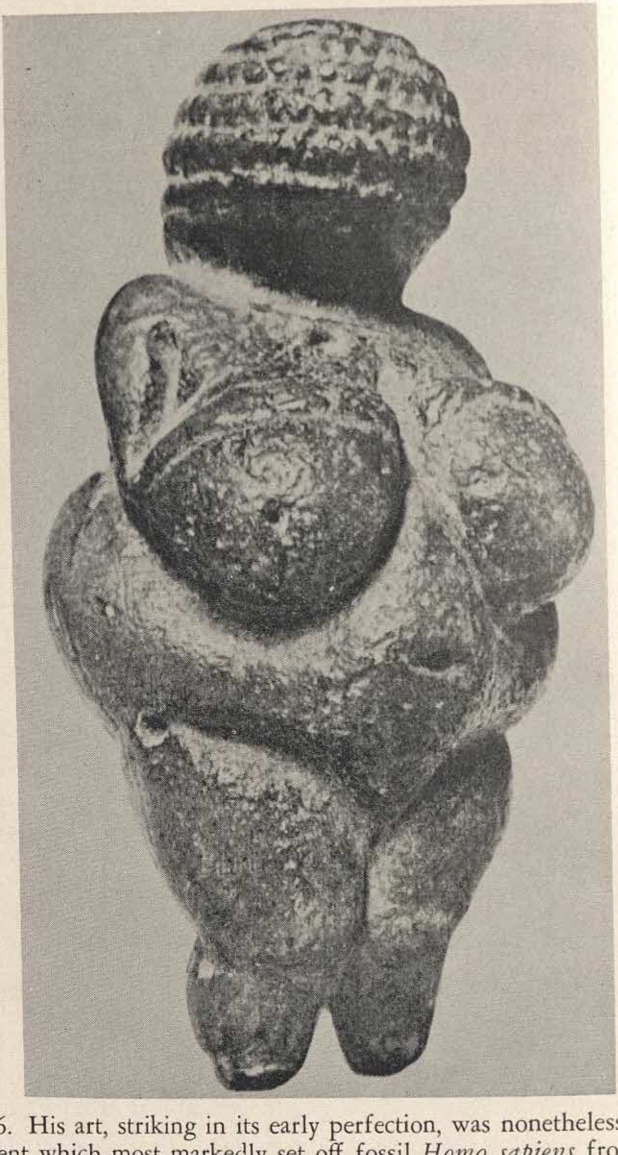

FIGURE 46. His art, striking in its early perfection, was nonetheless the cultural development which most markedly set off fossil *Homo sapiens* from his predecessors. While the animals he hunted were most often depicted, his interest in woman also found expression. In the four-inch high, limestone figurine, called the "Venus of Willendorf," the protuberant breasts, belly, buttocks and thighs have been proposed to emphasize an interest in fertility. Characteristically, the face is not depicted and, except for an elaborate coiffure, the head is a featureless globe. Frail and spindly arms and fingers, flexed upon the breasts, contrast with the robustness of the rest of the figure.

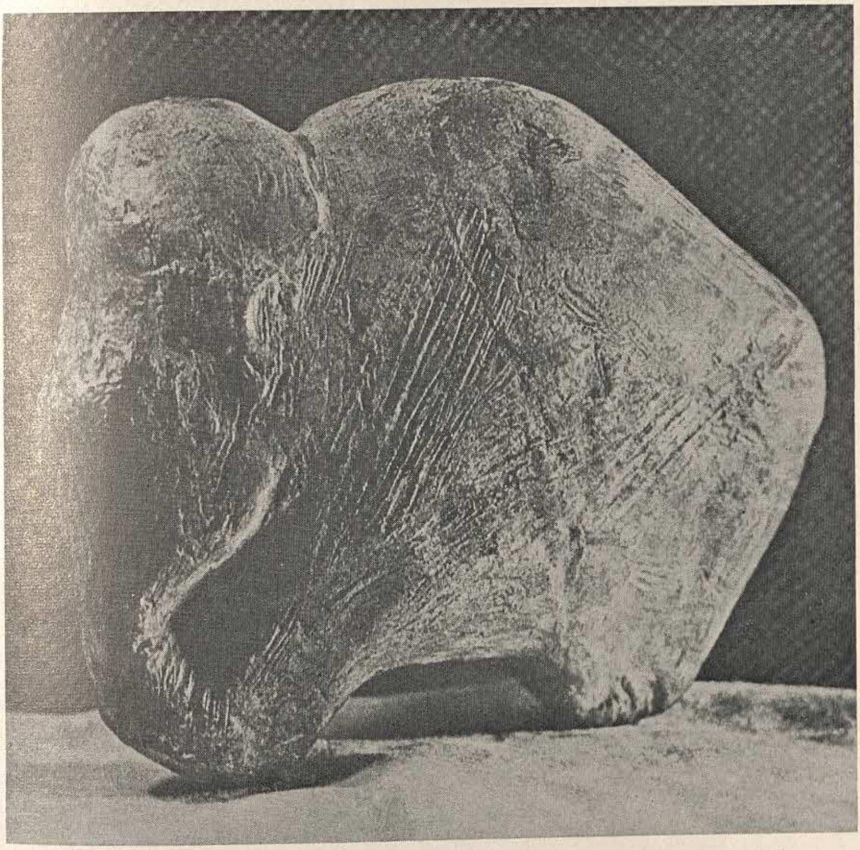

FIGURE 47. Most impressive of the animals hunted by Ice Age man was the now extinct mammoth, seen here in a stone carving from Brno, Czechoslovakia. The gigantic and now extinct creatures of an earlier age have always provided the most spectacular support for evolution in the popular mind. Because of their fantastic dimensions, the Dinosaur group of reptiles is obviously in first place. Though somewhat more modestly constituted, the mammoth runs a close second, the more particularly for its contemporaneity with prehistoric man. It is apparent that prehistoric man was himself impressed, for he carved the mammoth on its own ivory, drew and engraved it on the cave walls, and here sculptured it in statuette. In one of the cave drawings, the mammoth's heart is appropriately represented, the sole indication for a knowledge of internal anatomy on the part of fossil modern man.

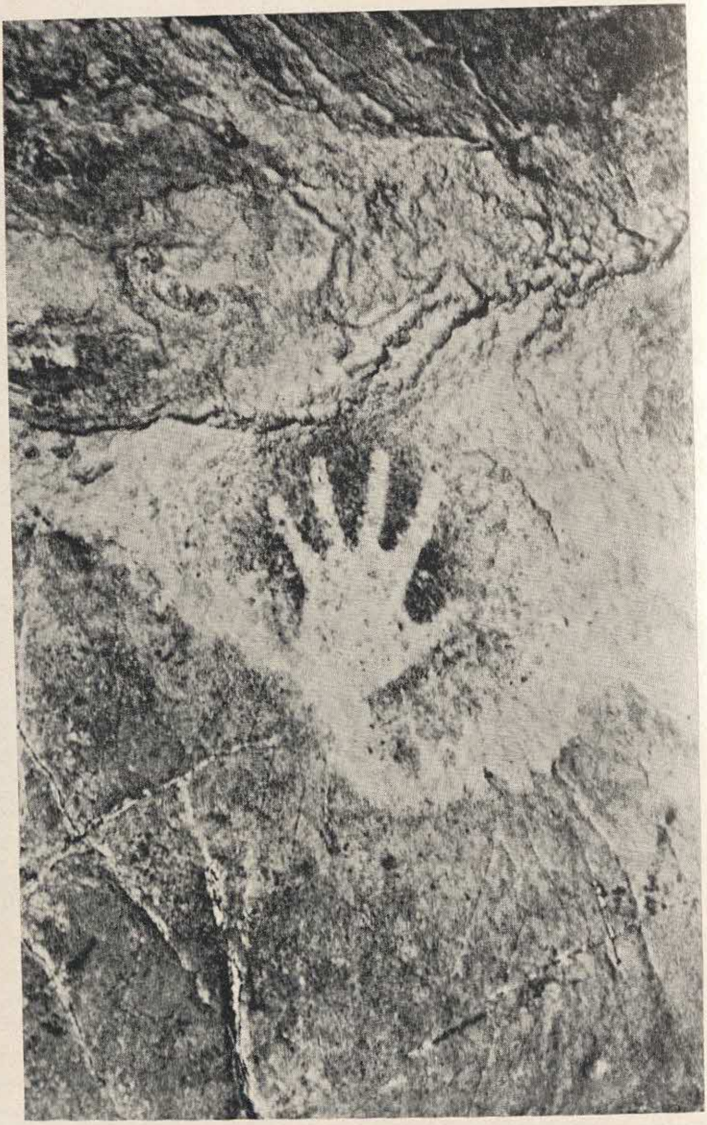

FIGURE 48. The greatest development of the artistic inclinations of Ice Age man are the cave paintings in Southern France and Spain. Not infrequently, the artist's own hand was represented, by holding one hand against the wall and applying pigment around it with the other. Because the left hand was most often depicted, it is presumed that right-handedness was already characteristic of fossil *Homo sapiens* and that left cerebral dominance had already developed. In some of the caves, one or more of the fingers were lacking in the paintings, suggesting ritualistic amputation.

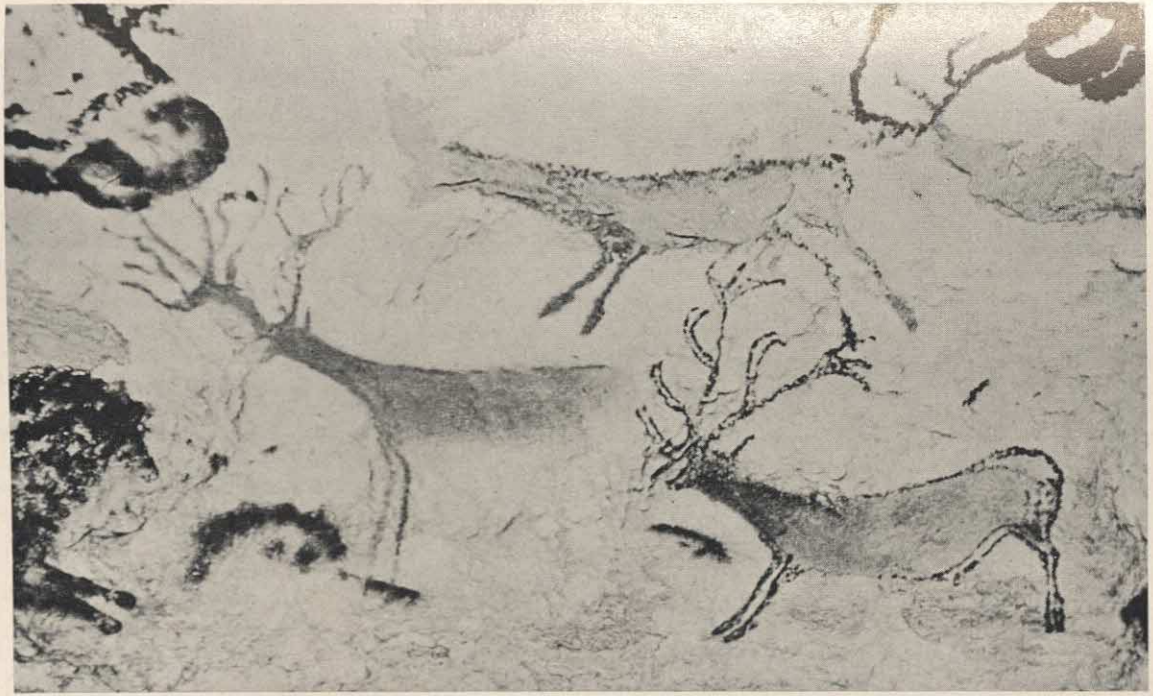

FIGURE 49. The reindeer were among the animals most frequently depicted on the cave walls by Ice Age man, and their bony remains are those most often found in the debris of his inhabited caves. Apparently, the reindeer formed his favorite game and provided his major food supply. Beside the mammoth and reindeer, the wild horse, bison, and rhinoceros, all important sources of food supply, were commonly painted in the caves. It is proposed that their depiction was ritualistic, as a kind of sympathetic magic to favor success in hunting, and spear thrusts in some of the figures support this view.

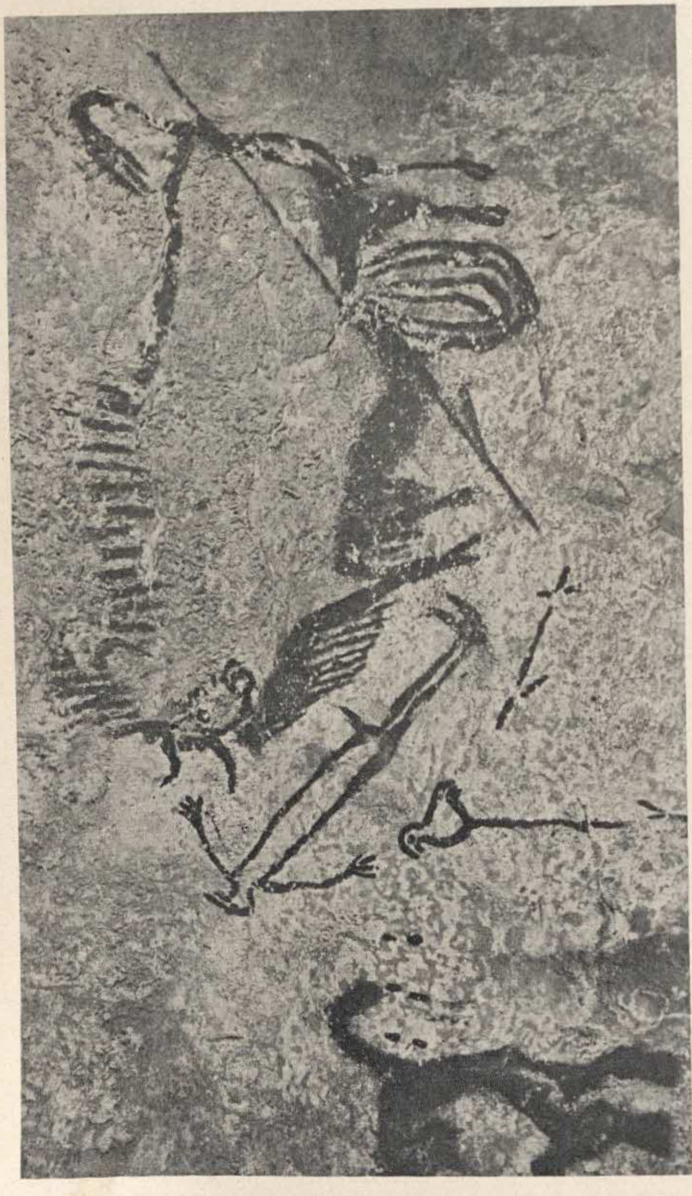

FIGURE 50. The debated "Dead Man Scene" in the Lascaux Cave in Southern France has been described by Abbé Breuil as "perhaps commemorating some fatal accident that occurred in the course of a hunt." The figures include a standing bison (right), lashing its tail and turning its head to examine a gaping abdominal wound, from which its entrails hang to the ground. A thinoceros (lower left) is moving rapidly out of the field. Between them, a man lies prone, masked as a bird, and exhibiting a conspicuous priapism. His spear is in the bison's wound, but the rhinoceros has apparently disemboweled the bison. The man may then have moved in for the kill, but was himself attacked and killed. Before him is a bird, perched on a rod, which may have been intended to represent his departing soul.

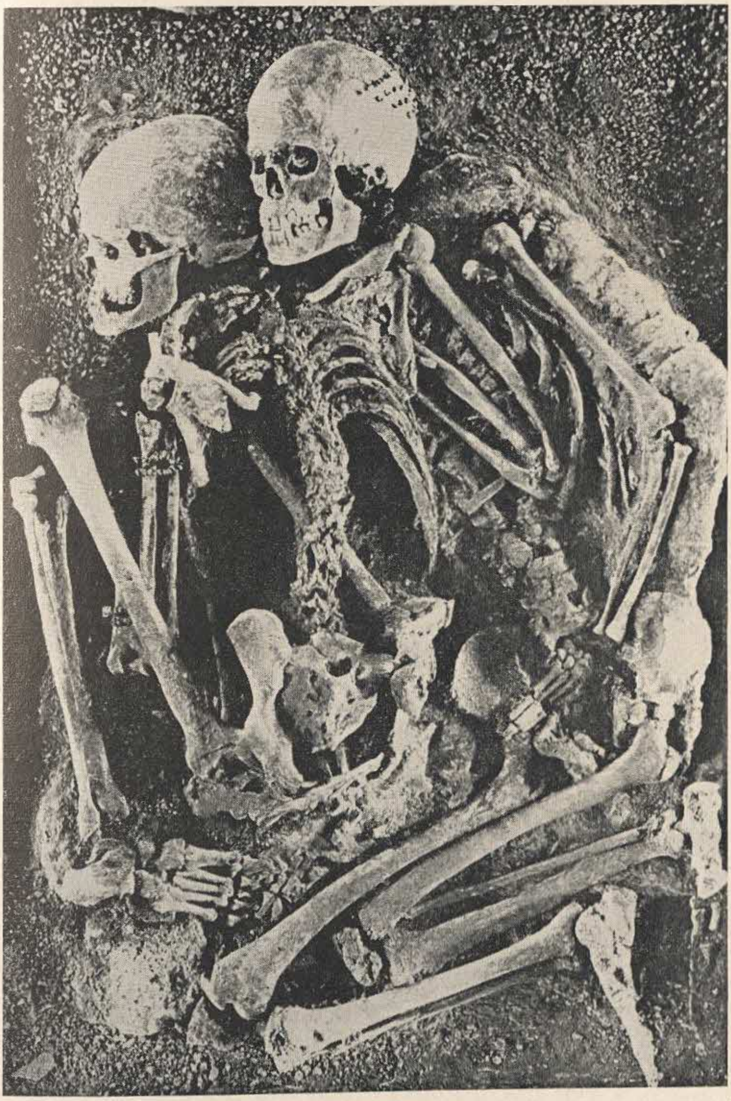

FIGURE 51. In addition to the ritualistic nature of his cave paintings, elaborate burial practices were introduced by fossil modern man. This grave at Grimaldi, on the Mediterranean Riviera, contained the embracing skeletons of an elderly female and an adolescent male, possibly mother and son. The youth was decorated with a headdress of shells. Red ochre pigment was scattered liberally over the grave. It has been suggested that this was a sort of powdered blood transfusion for a future life. Such finds provide insight into the psychology of primitive modern man. It is amazing how early was the development of concepts of magic, superstition, and the expectation of survival after death.

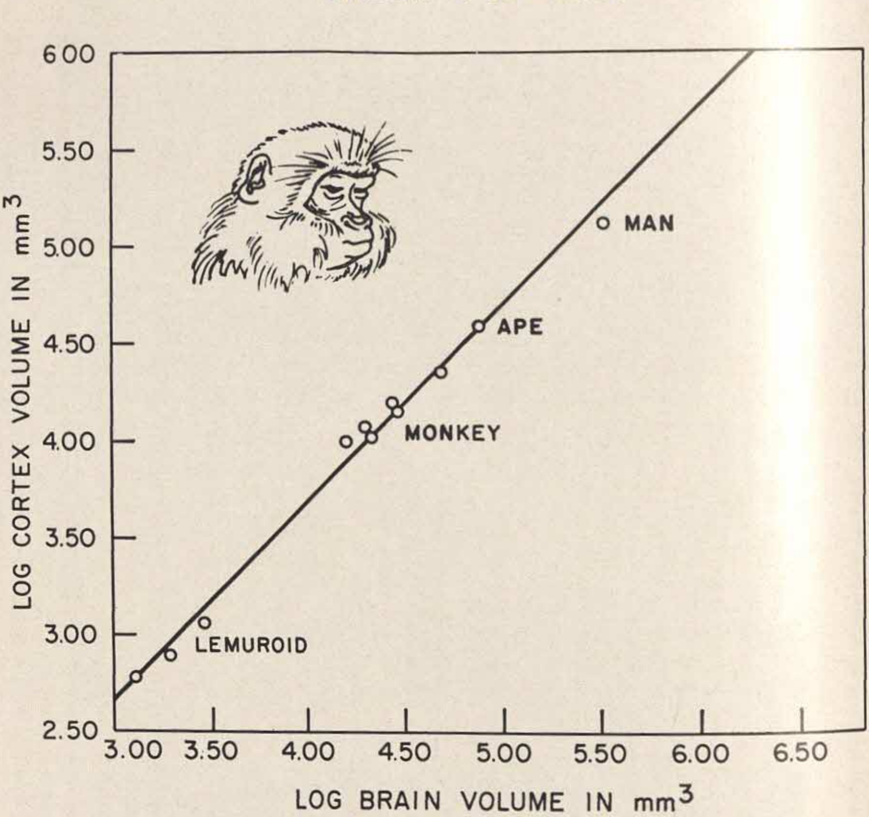

FIGURE 52. Within the order of mammals, the expanding neocortex exhibits an increasing proportion of the total volume of the brain. P. J. Harman has found that in rodents this cortex forms approximately 30 per cent of the total brain; in carnivores, 40 to 46 per cent; and in primates, 46 to 58 per cent. Within the primates, Harman's measurements have shown a linear increase in cortical volume, matching increase in the volume of the total brain. As the graph shows, three groups can be distinguished: lemuroids at the base (left); monkeys and apes in an intermediate position (center); and man at the top (right). It is of interest that the figure for the ape (chimpanzee) groups with those for monkeys, and is widely separated from that for man. Reprinted from Harman, P. J.: Aspects of Brain Phylogeny: *The James Arthur Lecture on The Evolution of the Human Brain.* American Museum of Natural History, New York, 1957.

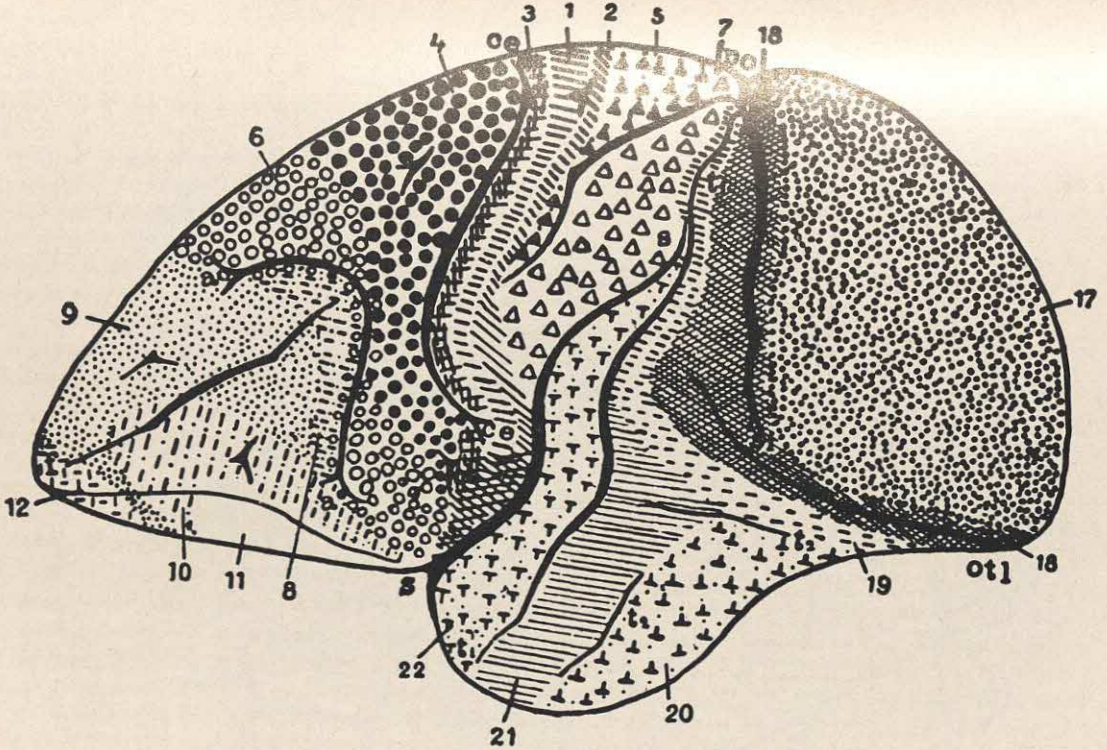

FIGURE 53. Brodmann's cytoarchitectural map shows the cortical areas of the monkey (Cercopithecus) in which the sensory and motor regions occupy far more space than the associational areas. Note that the visual cortex (area 17) is distributed chiefly on the lateral aspect of the hemisphere. Monkeys are often utilized in neurophysiological experiments with the notion that their brains resemble man's. Actually, the development of the associational cortex is quite rudimentary in the monkey by comparison with man. Reprinted from Brodmann, K.: Vergleichende Lokalizationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig, 1909.

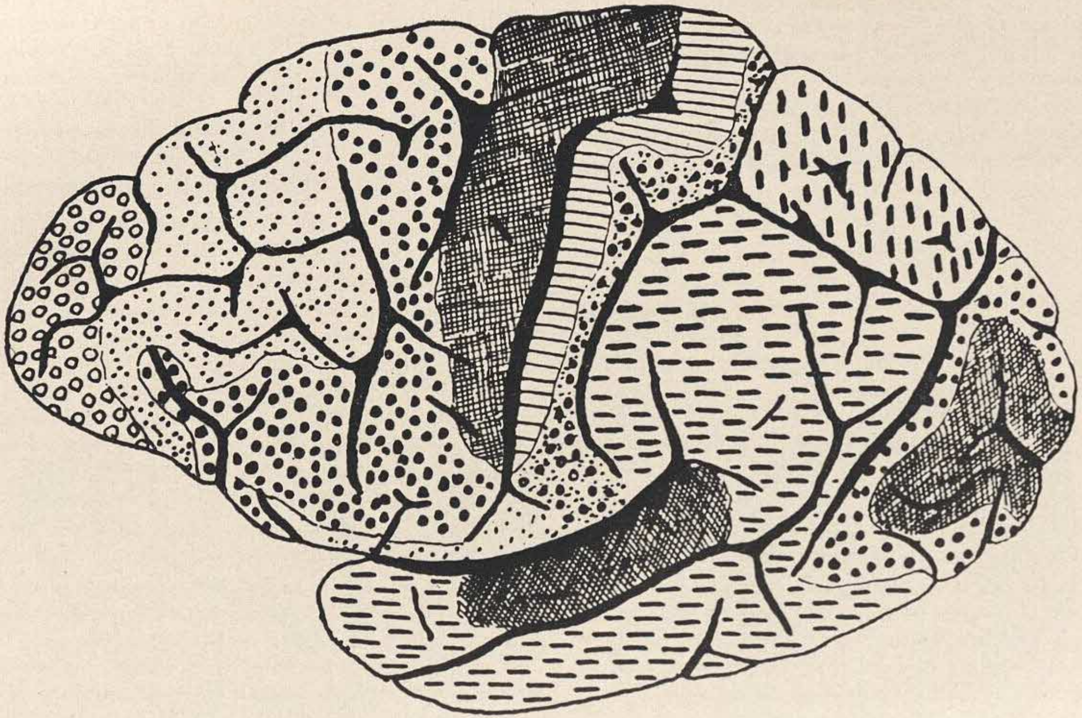

FIGURE 54. Campbell's map shows the cytoarchitectural cortical areas of the chimpanzee. The increasing development of the associational cortex has now separated the sensori-motor regions (shaded) from one another, and has pushed the visual cortex part way around the occipital pole on to the medial aspect of the hemisphere. At the turn of the century, Ferrier, Horsley, and Sherrington introduced the use of lower primates as experimental animals for brain research in England. Later, Fulton, Yerkes, and others continued this tradition in the United States, as did Pavlov later at Sukhumi in the USSR. The use of apes in research has continued to be rare, however. Currently, the National Institutes of Health have begun to support the establishment of primate research centers in the United States. Reprinted from Campbell, A. W.: *Histological Studies on the Localisation of Cerebral Function*, Cambridge University Press, 1905.

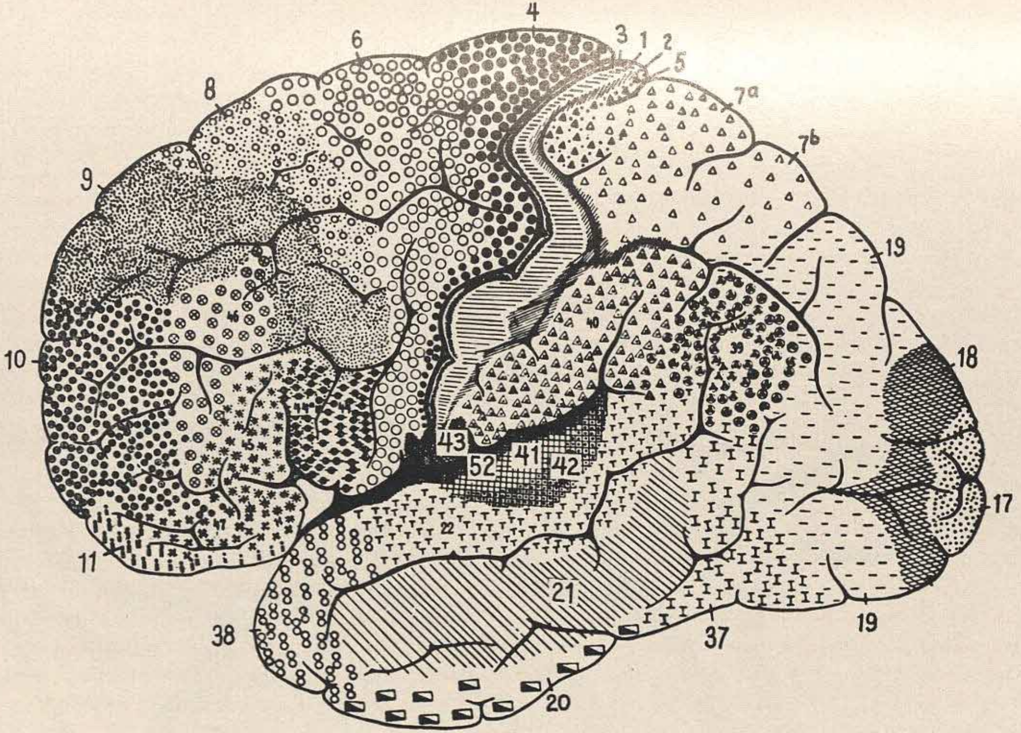

FIGURE 55. Brodmann's map shows the cytoarchitectural areas of the cerebral cortex of man. He studied serial horizontal sections of the hemisphere, beginning at the top, and numbered distinctive cytological fields as he went along. The lowest numbered areas, from 1 to 5, are thus located near the central region at the convexity and, in general, the numbers increase as one moves downward toward the base of the brain. In man, the massive development of associational cortex has crowded most of the somatic sensori-motor area into the central sulcus, the auditory area into the lateral fissure, and the visual area into the calcarine fissure on the medial aspect of the occipital lobe. Reprinted from Brodmann, K.: Vergleichende Lokalizationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig, 1909.

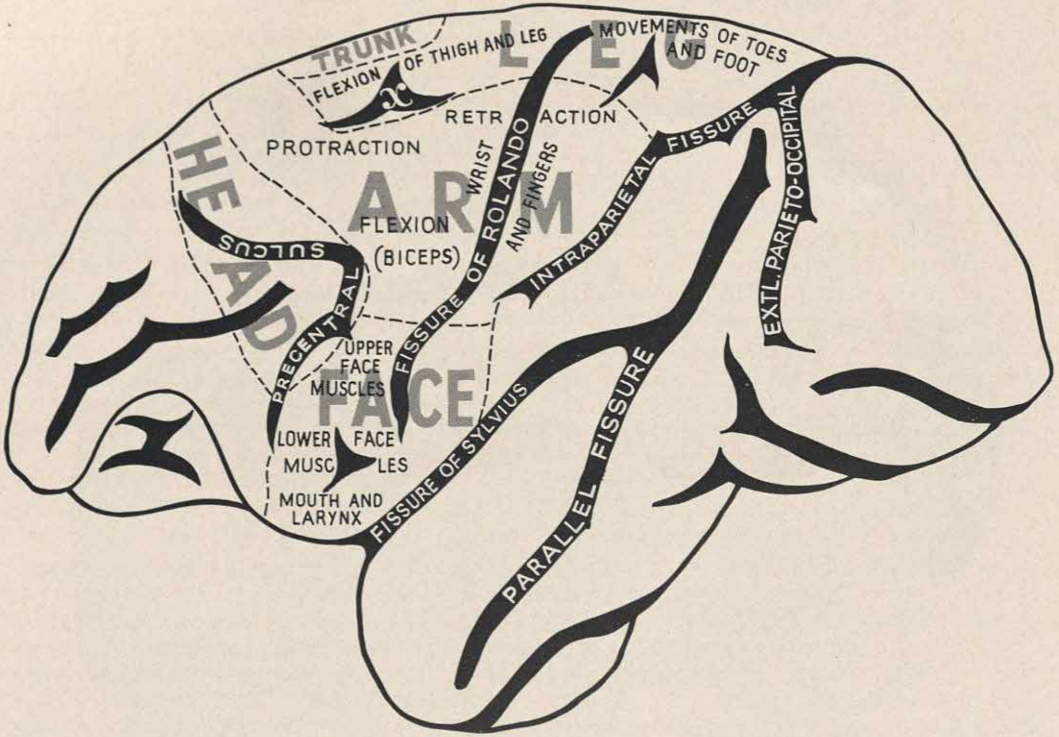

FIGURE 56. Discovery of the excitability of the motor cortex by Fritsch and Hitzig, in 1870, led to a large number of subsequent studies of electrical stimulation of the brain. Horsley's map of the somatotopic representation within the motor cortex of the monkey (*Macaca sinica*), published in 1888, shows the inversion of the body on the hemisphere with the lower extremity uppermost. Note also that the trunk and proximal limb musculature are represented anteriorly and the distal parts of the extremities posteriorly, in the central region. Approximately equal portions of the cortex are shown to be devoted to the representation of the leg, arm, and face. Reprinted from Horsley, V., and Schafer, E. A.: A record of experiments upon the functions of the cerebral cortex. *Phil. Trans Roy. Soc.* 179B: *1 (1888).*

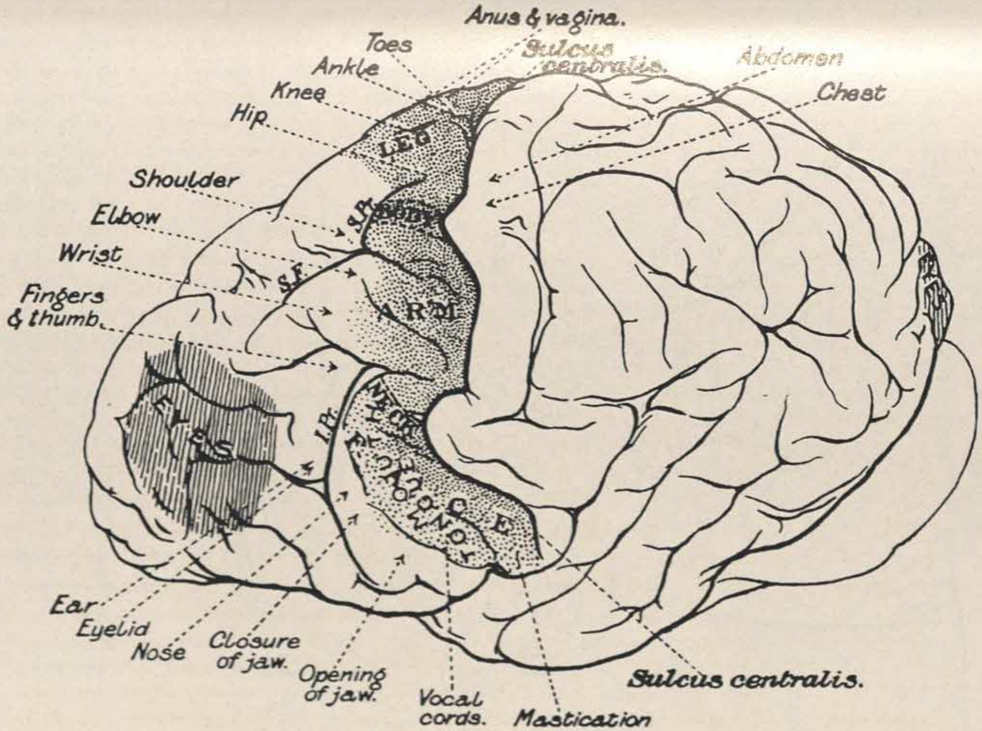

FIGURE 57. The first map showing somatotopic representation in the motor cortex of the chimpanzee was prepared by Grünbaum and Sherrington in 1903. Earlier, Hughlings Jackson's observations of clinical seizures beginning in the toe, thumb, or angle of the mouth, and spreading in a "march" to involve wider portions of the body, led him to postulate the existence of a motor cortex. The long-familiar hemiplegia following cerebral lesions supported this view. Ferrier's early demonstration of an hemiplegic monkey, following experimental ablation of the motor cortex, at a neurological congress in London at the turn of the century, caused Charcot to exclaim, "C'est une malade!" Reprinted from Grünbaum, A. S. F., and Sherrington, C. S.: Observations on the physiology of the cerebral cortex of the anthropoid apes. *Proc. Roy. Soc.* 72, *152 (1903).*

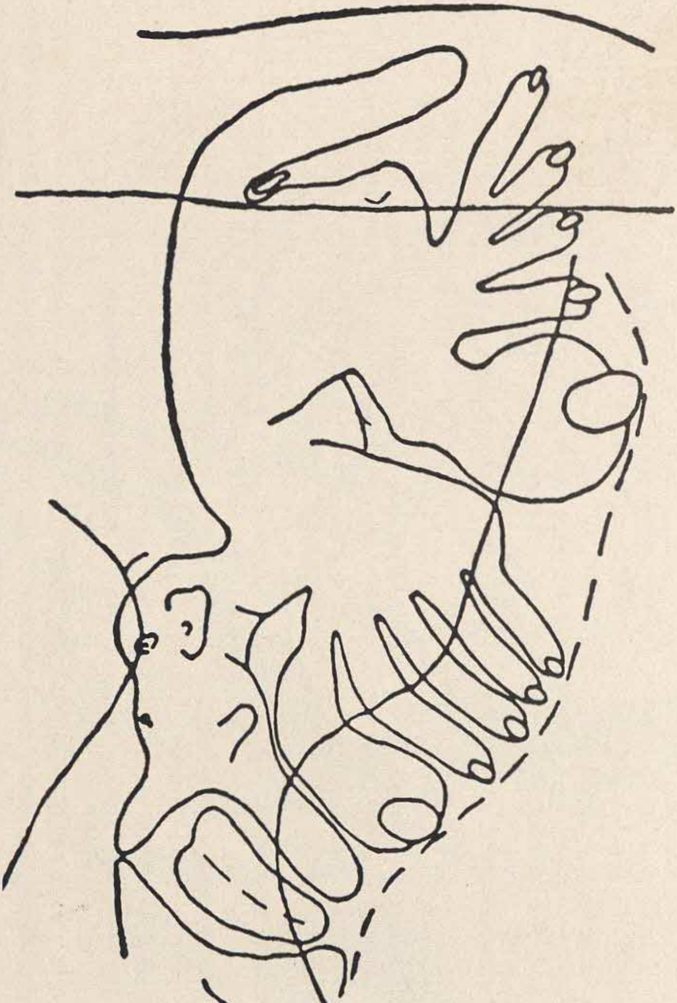

FIGURE 58. The most thorough recent study of somatotopic representation in the monkey's motor cortex has been undertaken by Woolsey and his associates. In this view of the central portion of the hemisphere of the Macaque monkey (compare Figures 53 and 56), Woolsey has constructed a "simunculus," the proportions of which reflect the extent of cortex devoted to each part. Note that the cortical region for movement of the foot is approximately as large as that for the hand, indicating the absence of functional specialization. In man, by contrast, the area for the hand has increased vastly over that for the entire lower extremity (Figure 59). Reprinted from Harlow, H. F., and Woolsey, C. N. (ed.): *Biological and Biochemical Bases of Behavior*. Madison, University of Wisconsin Press, 1958.

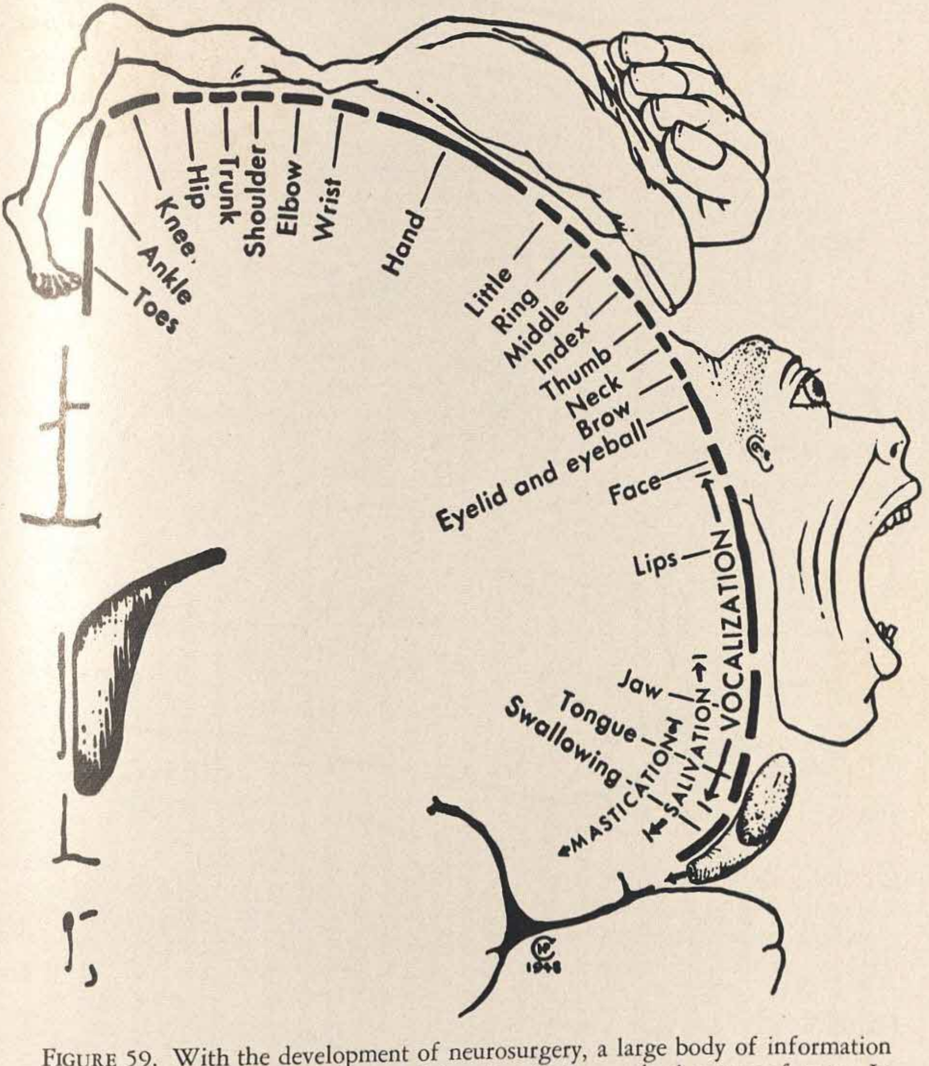

FIGURE 59. With the development of neurosurgery, a large body of information has been obtained on localization of function in the cerebral cortex of man. In this section through the cerebral hemisphere, Penfield, who has been the outstanding contemporary contributor to this field, has shown the representation of body parts in the motor cortex of man. The "homunculus" is grotesque because the dimension of the parts reflects the area of cortex devoted to their functions. The amount of cortex concerned with the hand, particularly its fingers, and most of all the opposable digit, the thumb, is as large as that for most of the rest of body and legs together. An equivalently large area is given to the face, in which the mouth, tongue, and larynx, concerned with speech, have the greatest representation. Reprinted from Penfield, W., and Rasmussen, T.: *The Cerebral Cortex of Man*. New York, Macmillan, 1950.

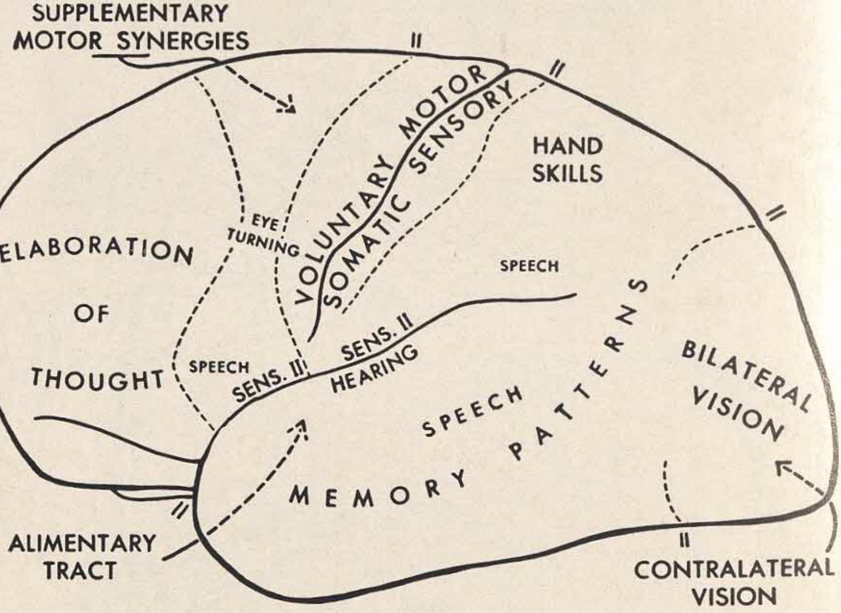

FIGURE 60. On this outline of the left cerebral hemisphere, Penfield has summarized the localization of cortical function, distilled from his long experience in study of the brain of man. In right-handed individuals, the left cerebral hemisphere is dominant, both in controlling the hand and in containing the neural representation for the management of speech. The localization of cortical speech areas is visible in the inferior frontal region, ahead of the motor region for the face, as well as in the inferior parietal and temporal lobes, adjacent to the cortical sensory areas for hearing and vision. The long period of their postnatal maturation is shown in Figure 73. Reprinted from Penfield, W., and Jasper, H. H.: *Epilepsy and the Functional Anatomy of the Human Brain.* Boston, Little, Brown, 1954.

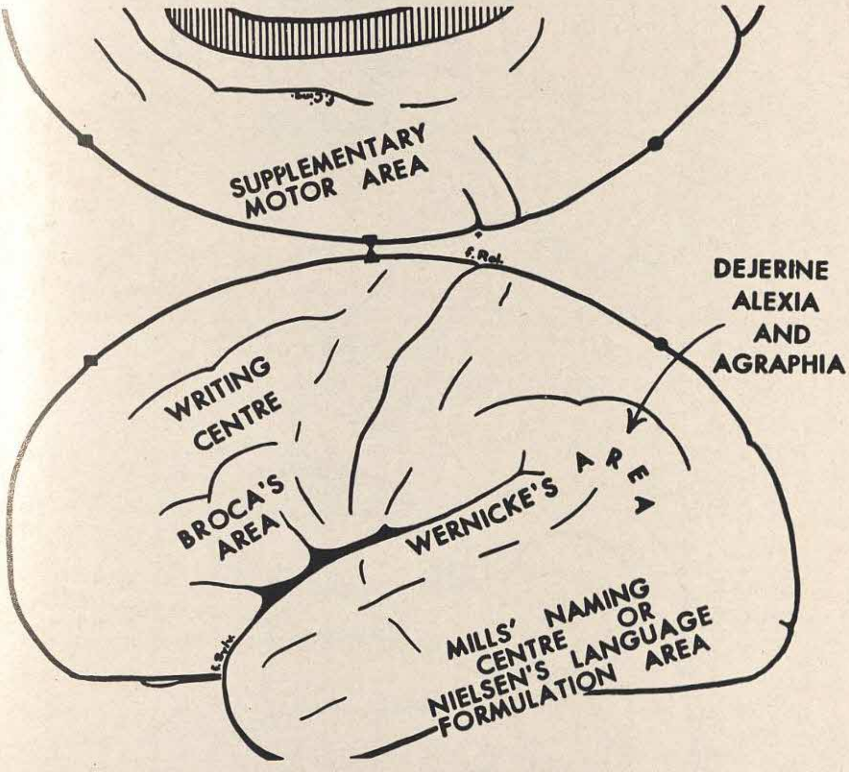
SUPPLEMENTARY MOTOR AREA
f. Rol.
DEJERINE ALEXIA AND AGRAPHIA
WRITING CENTRE
BROCA'S AREA
WERNICKE'S AREA
MILLS' NAMING CENTRE OR NIELSEN'S LANGUAGE FORMULATION AREA
f. Sylv.

FIGURE 61. The cortical speech areas, as taken from the literature, are represented in this outline of the left or dominant cerebral hemisphere. Writing and vocal speech are managed by the frontal cortex, ahead of the hand and face portions of the motor region proper. This inferior frontal focus for motor speech was discovered by Paul Broca, the distinguished French anthropologist who described Cro-Magnon man. The inferior parietal and temporal speech areas were differentiated by Wernicke, Dejerine, Head, Mills, Nielsen, and others. Injury to these areas in the dominant hemisphere is followed by sensory, motor, or mixed types of aphasia. Similar injury on the opposite or recessive side of the brain does not result in speech impairment. Reprinted from Penfield, W., and Roberts, L.: *Speech and Brain Mechanisms*. Princeton, Princeton University Press, 1959.

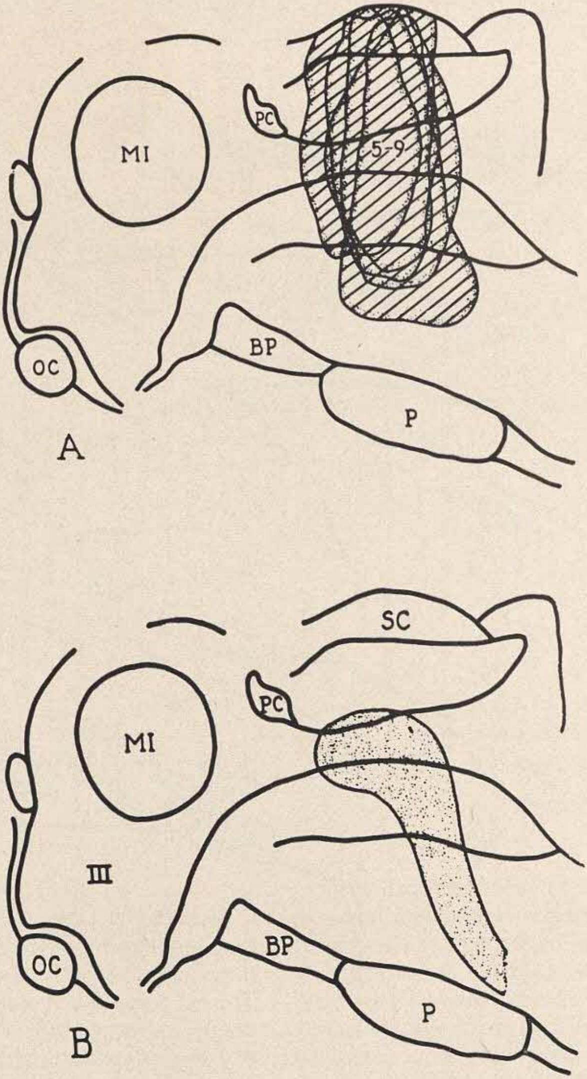

FIGURE 62. While communication by means of spoken or written symbols is managed by associational areas of the dominant cerebral hemisphere, developed only in man, facio-vocal behavior in the expression of emotion is widely represented in animal forms and is managed by mechanisms in the brain stem. In these views of the midplane of the cat's brain stem, shading indicates (B) the region from which facio-vocal responses may be evoked by stimulation and (A) the distribution of lesions which greatly reduced or abolished facio-visual activity in emotional behavior in several animals. Reprinted from Kelly, A. H., Beaton, L. E., and Magoun, H. W.: A midbrain mechanism for facio-vocal activity. *J. Neurophysiol.* **9,** *181 (1946).*

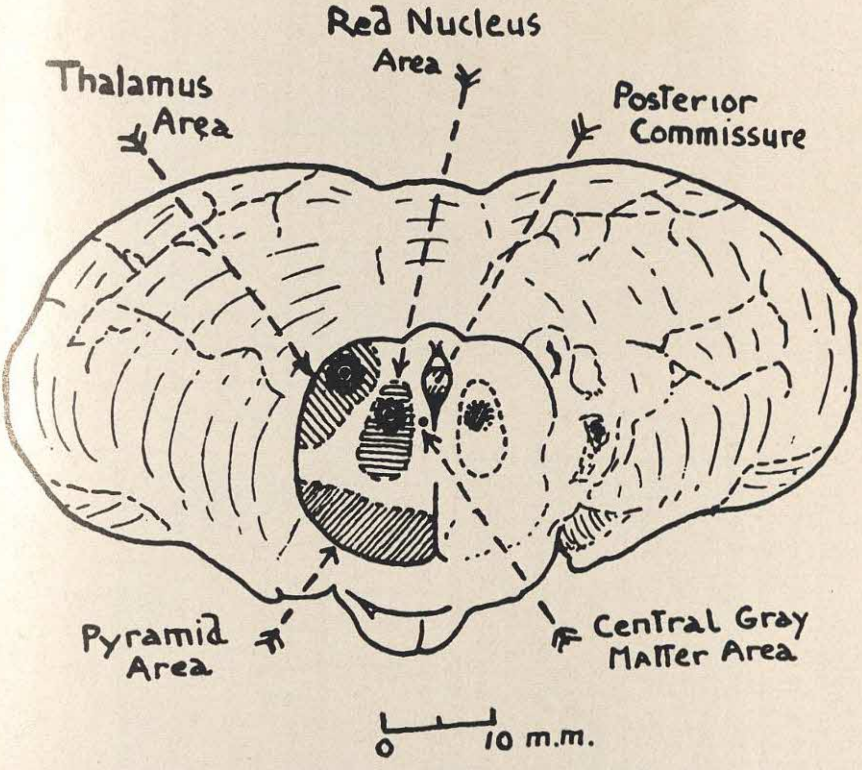

FIGURE 63. The subcortical management of emotional vocalization was first proposed by Graham Brown (1914) in his study of the decerebrate chimpanzee. After removal of all higher parts of the brain, stimulation of the surface of the mesencephalon, at the point marked "central grey matter," evoked a facio-vocal response resembling "the act of laughter." The subcortical mechanism for facio-vocal expression of emotion is present in man as well as in animals. Mesencephalic lesions may reduce or abolish such behavior in man without impairment of symbolic speech. Conversely, bilateral injury of the face portion of the motor cortex in man leads to pseudobulbar palsy, with pathologically exaggerated laughter or crying, conceived as release of deep-lying functions from cortical inhibition. Reprinted from Brown, G.: Note on the physiology of the basal ganglia and midbrain of the anthropoid ape, especially in reference to the act of laughter. *J. Physiol.* 49, *195 (1914).*

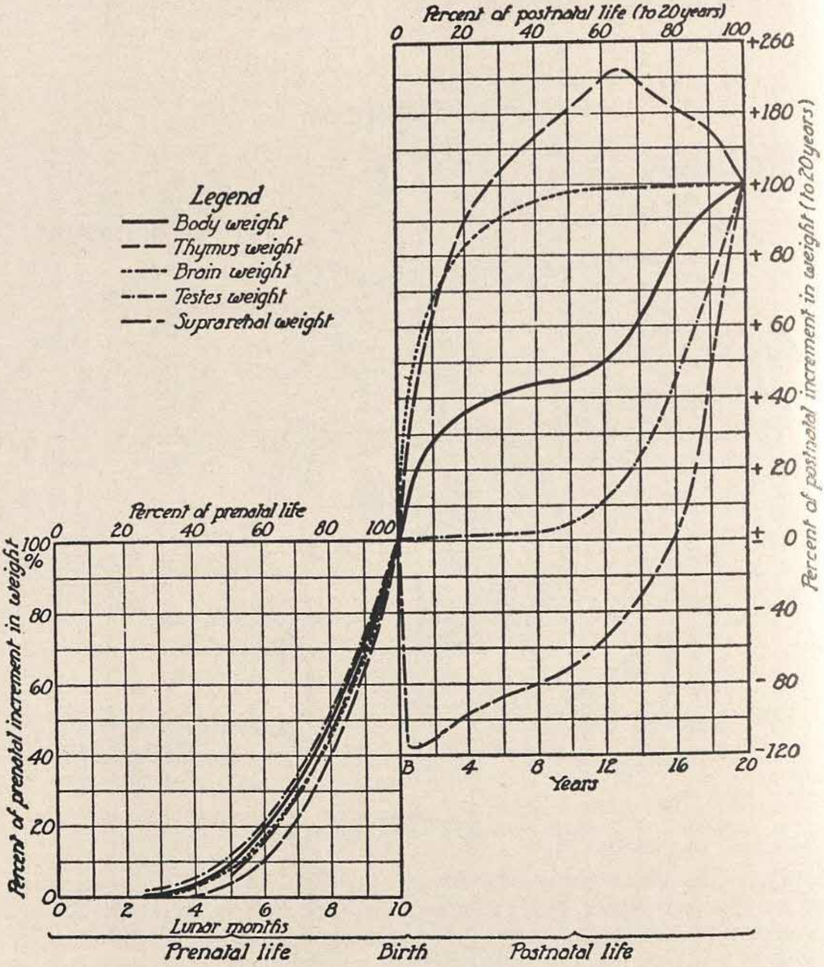

FIGURE 64. Graphs of prenatal and postnatal rates of growth of several structures of man's body indicate that the prenatal growth of the brain closely parallels that of other organs. Following birth, however, the brain becomes the most rapidly growing organ of the body. During the first three postnatal years, its expansion is matched only by that of the thymus gland. In its remarkable postnatal growth, the brain gains half of its adult weight by the end of the first year, three-quarters by the age of 3 years, and 90 per cent by the age of 6 years. By the age of 10, it has practically gained its adult weight, though there is a slight, additional increment to the age of 20 years. Reprinted from studies by Scammon, R. E., in Harris, J. A.: *The Measurement of Man*. Minneapolis, University of Minnesota Press, 1930.

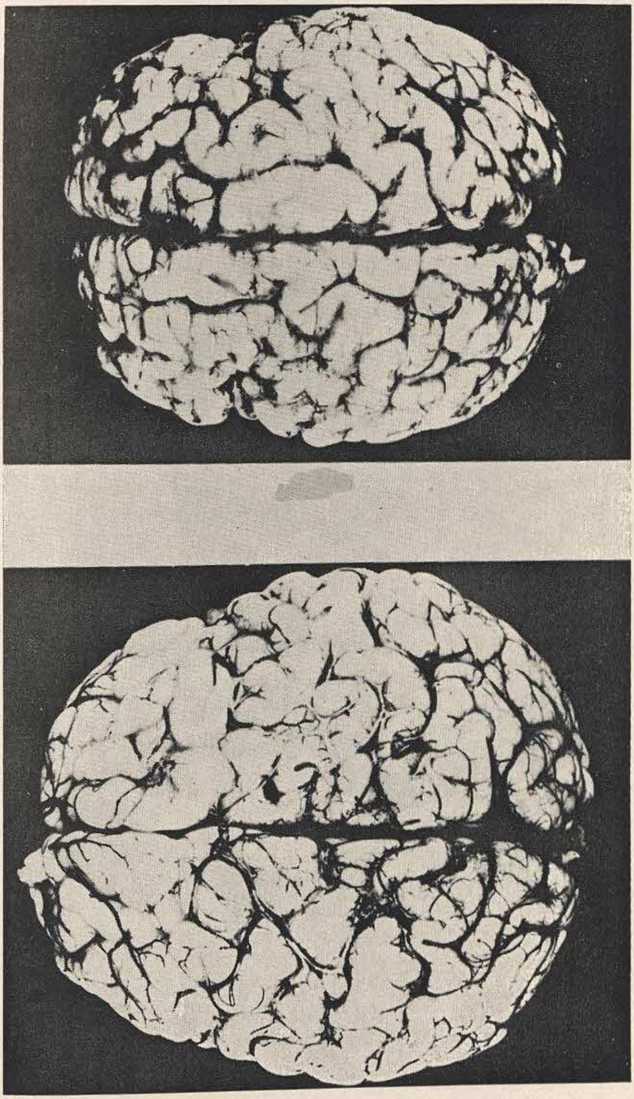

FIGURE 65. Photographs of the human brain at birth (above) and at 3 months of age (below) show its rapid postnatal growth. In this brief period of time, its weight has increased from 380 to 550 gm. While postnatal growth of other organs occurs by multiplication of constituent cells, the total number of neurons in the central nervous system is presumed to have been gained before birth. Succeeding changes are attributable only to maturation of already existing nerve cells, or to multiplication of neuroglia, which have been little studied. Reprinted from Conel, J. L.: *The Post-Natal Development of the Human Cerebral Cortex*. Cambridge, Harvard University Press, 1939-55.

## Absolute Weight of the Organs in Man
(gm)

| Age | No. of Cases | Brain | No. of Cases | Heart | No. of Cases | Right Lung | No. of Cases | Left Lung | No. of Cases | Liver | No. of Cases | Kidneys | No. of Cases | Spleen |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 Months | 36 | 381 | 61 | 23.6 | 52 | 30.2 | 52 | 23.9 | 10 | 141.7 | 13 | 23.3 | 10 | 10.6 |
| 1 | 5 | 463.8 | 7 | 17.2 | 2 | 26 | 2 | 27.5 | 2 | 100.5 | 2 | 26 | 2 | 10 |
| 2 3 | 8 | 548.9 | 30 | 17.1 | — | — | — | — | 3 | 132.3 | 3 | 30.1 | 3 | 11 |
| 4 5 6 | 7 | 632.4 | 27 | 22.6 | 11 | 42.3 | 11 | 45 | 5 | 148.7 | 6 | 44.1 | 5 | 13.5 |
| 7 8 9 | 5 | 740 | 28 | 29.4 | 3 | 62.3 | 3 | 53 | 5 | 219.2 | 4 | 46.7 | 4 | 16.5 |
| 10 11 | — | — | 6 | 33.74 | 1 | 102.8 | — | — | 1 | 404 | 1 | 53.1 | — | — |
| 1 Year | 17 | 944.7 | 15 | 41.2 | 10 | 83 | 11 | 73.6 | 11 | 333.3 | 11 | 72.8 | 10 | 20.3 |
| 1¼ | 1 | 782 | 1 | 44.4 | — | — | — | — | — | — | 1 | 54.5 | — | — |
| 1½ | 3 | 1019.7 | 1 | 47.5 | — | — | — | — | 2 | 333.5 | 4 | 72.8 | 2 | 30.5 |
| 1¾ | 1 | 1078 | 3 | 46.5 | — | — | — | — | 1 | 412 | 2 | 80.5 | 2 | 31 |
| 2 | 27 | 1025.4 | 45 | 51.9 | 27 | 101.5 | 27 | 82.1 | 28 | 428.2 | 28 | 90.6 | 26 | 43.2 |
| 2½ | 2 | 1159.5 | 2 | 53.3 | 2 | 137 | — | — | — | — | 3 | 121.4 | — | — |
| 3 | 19 | 1108.1 | 30 | 64.8 | 15 | 138.3 | 15 | 118.1 | 17 | 484.7 | 18 | 102.1 | 16 | 45.9 |
| 3½ | 1 | 1249.5 | 1 | 57.7 | — | — | — | — | — | — | 1 | 100.8 | — | — |
| 4 | 19 | 1330.1 | 31 | 74.1 | 18 | 156.5 | 19 | 147.4 | 18 | 588.5 | 23 | 107.7 | 16 | 52.9 |
| 5 | 16 | 1263.4 | 19 | 81 | 13 | 130 | 15 | 110.6 | 15 | 538.8 | 14 | 114.6 | 13 | 57.2 |
| 6 | 10 | 1359.1 | 6 | 84.9 | — | — | — | — | 5 | 614.8 | 7 | 106.8 | 4 | 60 |
| 7 | 14 | 1348.4 | 18 | 93.3 | 11 | 189.9 | 11 | 172 | 11 | 688 | 12 | 128.3 | 10 | 62.6 |
| 8 | 4 | 1377.6 | 3 | 95 | — | — | — | — | 2 | 650 | 3 | 126.8 | 2 | 62.5 |
| 9 | 3 | 1425 | 6 | 108.3 | 3 | 190 | 3 | 167.5 | 4 | 701.7 | 5 | 156 | 3 | 62.5 |
| 10 | 8 | 1408.3 | 9 | 127.7 | 6 | 236.3 | 6 | 250.6 | 7 | 836.7 | 8 | 160.8 | 5 | 87.8 |
| 11 | 7 | 1359.9 | 11 | 140.9 | 7 | 236.4 | 7 | 229.5 | 9 | 870.4 | 8 | 171.5 | 8 | 71.3 |
| 12 | 5 | 1415.6 | (1 | 97.5) | 3 | 240 | 3 | 175 | 3 | 880 | 3 | 157.5 | 3 | 70 |
| 13 | 8 | 1486.5 | 7 | 164 | 5 | 249.9 | 4 | 208.8 | 6 | 1036 | 6 | 212.9 | 5 | 86 |
| 14 | 12 | 1289 | 8 | 216.1 | 7 | 414.6 | 7 | 283.5 | 7 | 1188.7 | 7 | 233.7 | 4 | 70 |
| 15 | 3 | 1490.2 | 7 | 199.4 | 5 | 382.6 | 4 | 367.7 | 5 | 1306 | 5 | 239.7 | 3 | 145 |
| 16 | 7 | 1435.1 | 11 | 229.4 | 9 | 419.5 | 9 | 327.8 | 10 | 1339.2 | 10 | 247.7 | 10 | 153.7 |
| 17 | 15 | 1409.2 | 17 | 250.9 | 11 | 429.9 | 11 | 343 | 12 | 1481.5 | 14 | 274.9 | 12 | 145.6 |
| 18 | 18 | 1421 | 16 | 243.1 | 13 | 485 | 13 | 382 | 13 | 1509.6 | 11 | 271.6 | 13 | 176.2 |
| 19 | 21 | 1397.2 | 20 | 293.1 | 15 | 533.8 | 14 | 456.7 | 15 | 1644.6 | 14 | 273.9 | 10 | 166 |
| 20 | 14 | 1444.5 | 15 | 305.3 | 9 | 513.6 | 9 | 448.9 | 11 | 1560.8 | 11 | 296.4 | 2 | 186.2 |
| 21 | 29 | 1412.1 | 26 | 297.1 | 20 | 486.5 | 20 | 457.4 | 21 | 1626.9 | 22 | 323.5 | 23 | 168.1 |
| 22 | 26 | 1348.3 | 24 | 312.5 | 19 | 526.2 | 17 | 472.1 | 20 | 1675 | 21 | 306.9 | 18 | 148.9 |
| 23 | 22 | 1397.3 | 22 | 292.9 | 16 | 510 | 16 | 436 | 17 | 1528.3 | 18 | 281.8 | 16 | 153.7 |
| 24 | 30 | 1423.9 | 28 | 308.8 | 20 | 524.4 | 20 | 437.4 | 22 | 1847.7 | 22 | 289.5 | 23 | 177.4 |
| 25 | 25 | 1430.9 | 28 | 300.6 | 17 | 512.6 | 20 | 482.3 | 17 | 1819 | 18 | 305.9 | 15 | 163.0 |
| Total Cases | 448 |  | 590 |  | 350 |  | 346 |  | 336 |  | 361 |  | 298 |  |

FIGURE 66. This table from Vierordt shows the increase of weight of the brain and other organs of the body with age. Histological study has identified two categories of postnatal neuronal maturation in the central nervous system. One consists of the development of a myelin sheath, interrupted at nodes, around the transmitting axon of the nerve cell. The other involves the multiplication and extension of synapse-bearing dendrites, spreading out from the neuron's soma. Translated from Vierordt, H.: Das Massenwachsthum der Korperorgane des Menschen. *Arch. f. Anat. u. Physiol. Anat. Abth. s 62 (1890).*

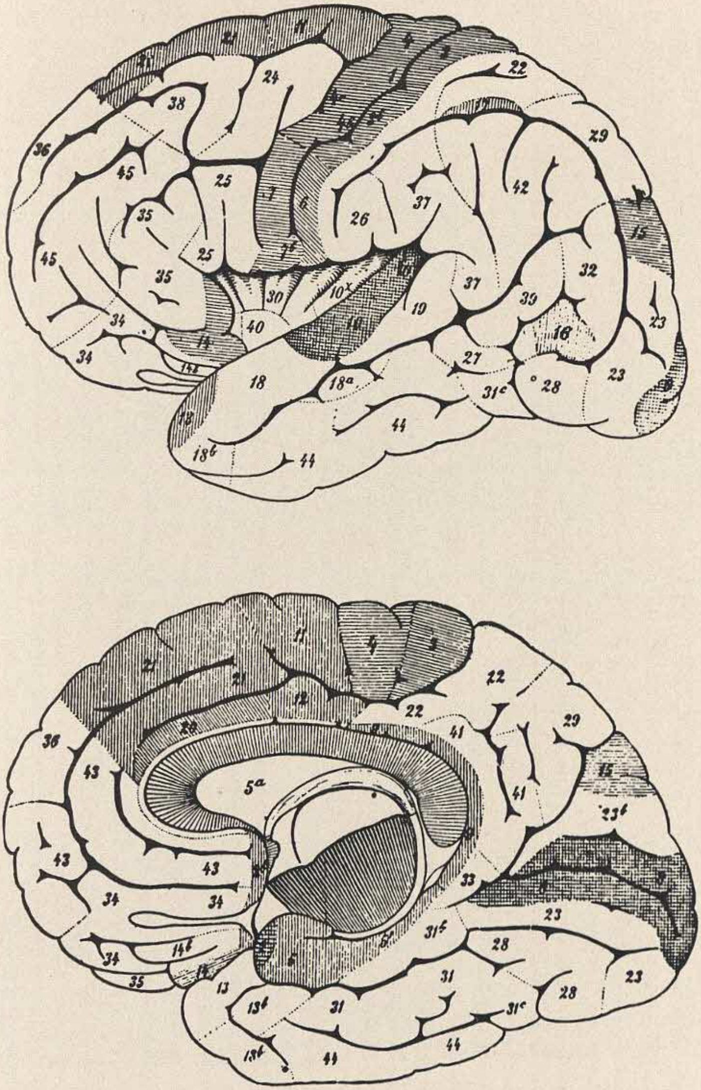

FIGURE 67. Lateral and medial views of the adult cerebral hemisphere of man show the order of cortical myelinization during development of the brain. The numbers indicate the sequence in which cortical regions acquire myelin sheaths. The sensori-motor areas (shaded) mature first, and the associational regions later, corresponding to their respective order of functional maturation after birth. Growth of a nodal, myelin sheath favors the velocity of saltatory conduction along the axon of a brief, all-or-none, spike potential, followed by refractoriness. Reprinted from Flechsig, P.: *Anatomie des menschlichen Gehirns und Ruckenmarks auf myelogenetisches Grundlage*. Leipzig, G. Thieme, 1920.

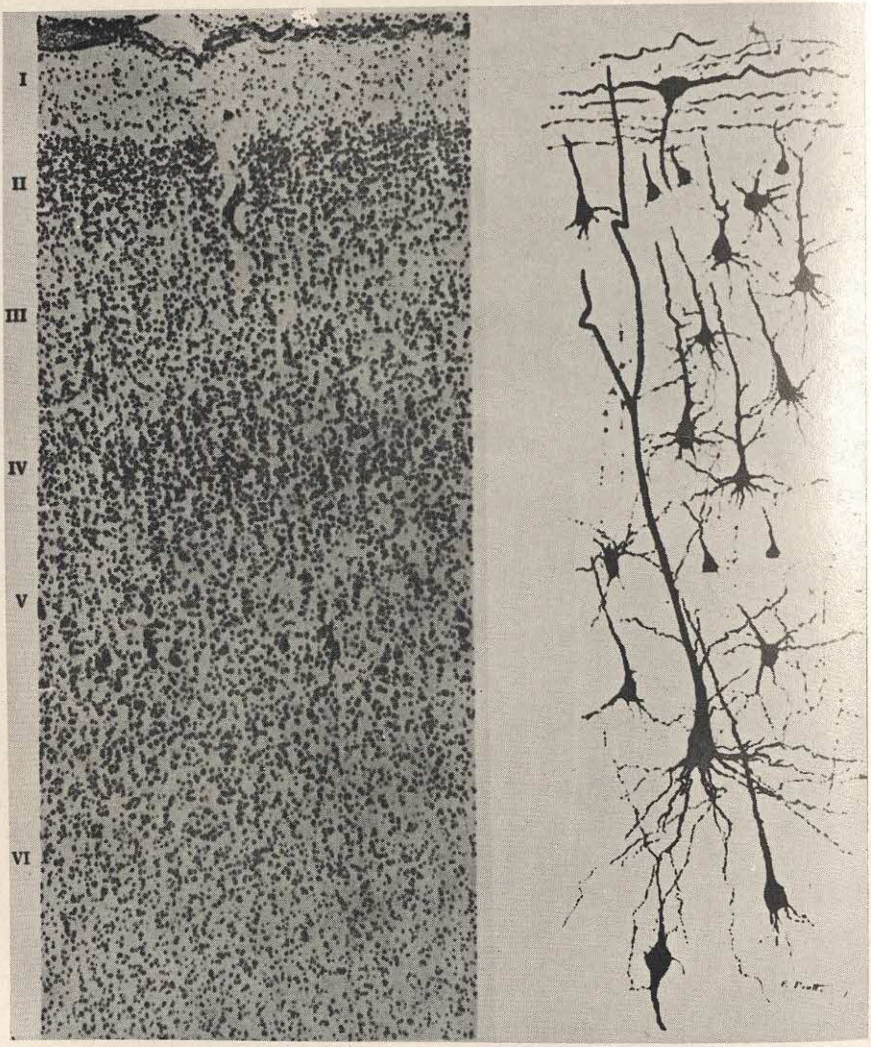

FIGURE 68. Cresyl-violet (left) and Golgi (right) stained sections, through the hand area of the motor cortex, at birth. When compared with those in Figure 69, these show the expansion of all cortical layers by 3 months of age. In the Golgi stained sections, it is evident that the apical dendrites of the cortical pyramidal cells are already prominently developed at birth. Their terminal branches, however, and especially the basal dendritic plexus, undergo great expansion by 3 months of age. Reprinted from Conel, J. L.: *The Post-Natal Development of the Human Cerebral Cortex*. Cambridge, Harvard University Press, 1939-55.

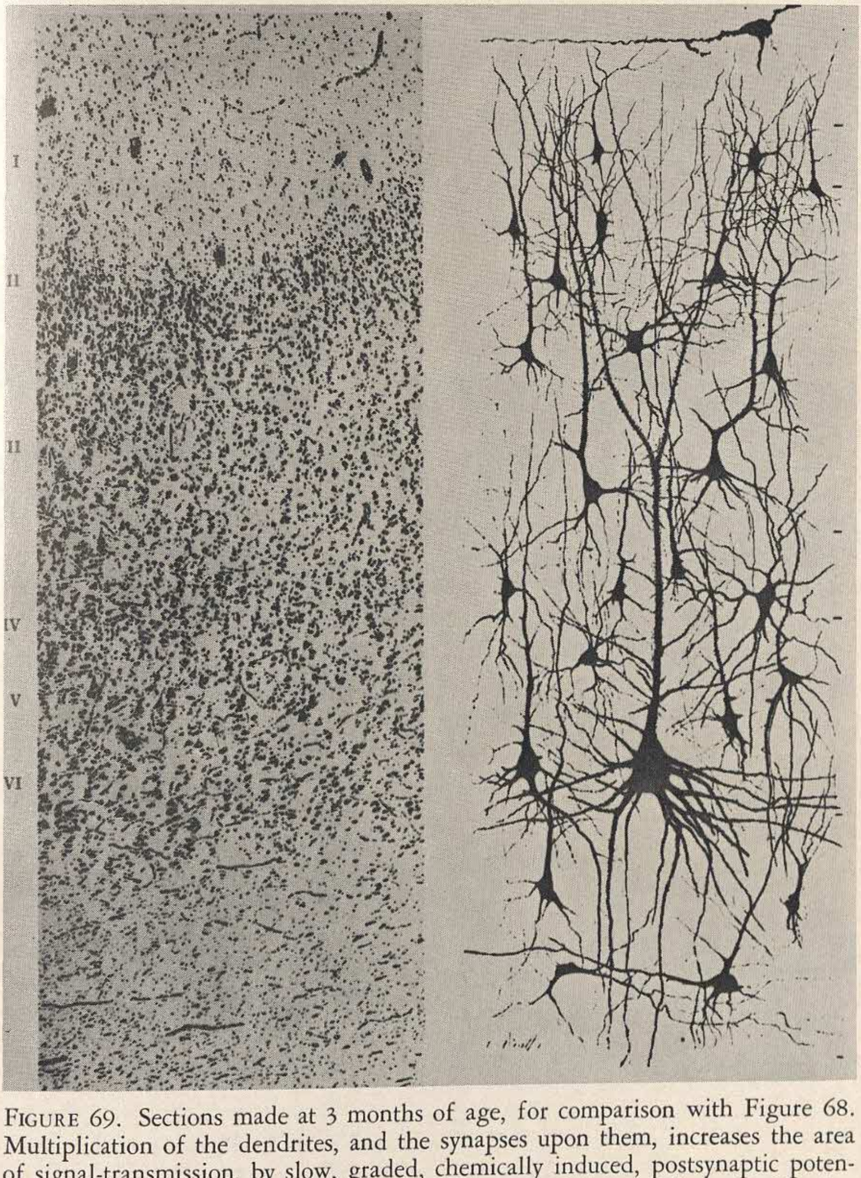

FIGURE 69. Sections made at 3 months of age, for comparison with Figure 68. Multiplication of the dendrites, and the synapses upon them, increases the area of signal-transmission, by slow, graded, chemically induced, postsynaptic potentials, determining the threshold for excitation or inhibition of the conducting soma-axonal portion of the cell. Reprinted from Conel, J. L.: *The Post-Natal Development of the Human Cerebral Cortex*. Cambridge, Harvard University Press, 1939-55.

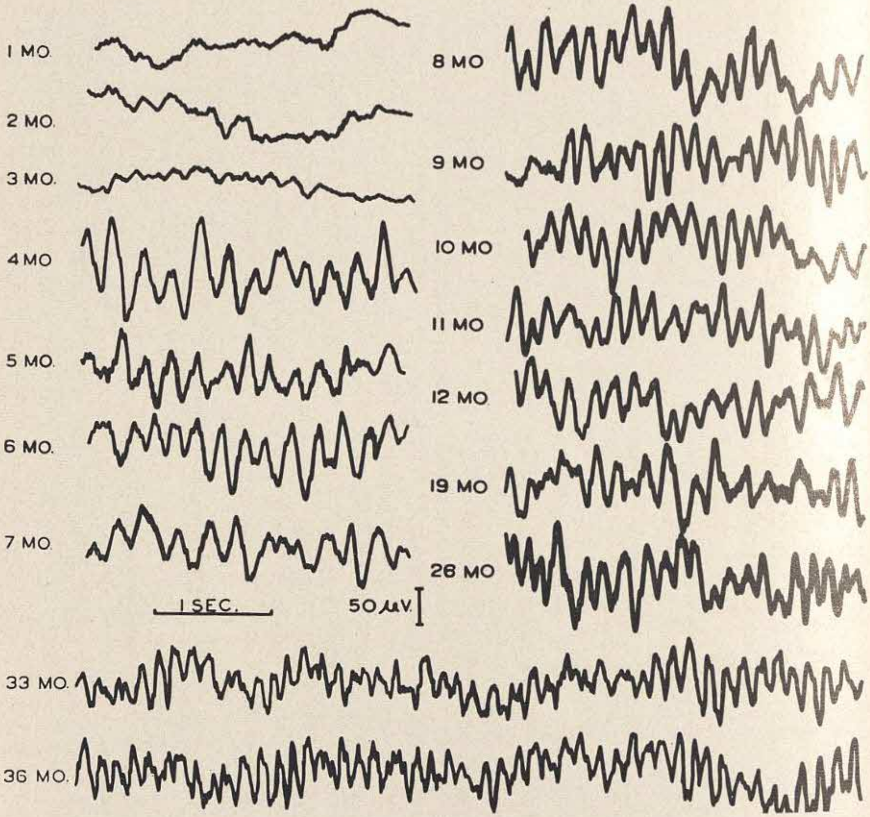

FIGURE 70. Serial tracings show the gradual maturation of the human EEG. Occipital records were taken at postnatal stages between 1 and 36 months. Little organized activity could be recorded in the first 3 months. Rhythmic alterations in potential, of slow rate and high amplitude, then appeared at 4 months, and gradually attained characteristics of the adult $\alpha$-rhythm. While full maturation of the $\alpha$-rhythm was not seen until 3 years of age, its earlier appearance is correlated with the development of graded response mechanisms in cortical dendrites. Reprinted from Lindsley, D. B.: A longitudinal study of the occipital alpha rhythm in normal children. *J. Genet. Psychol.* **55**, *197 (1939).*

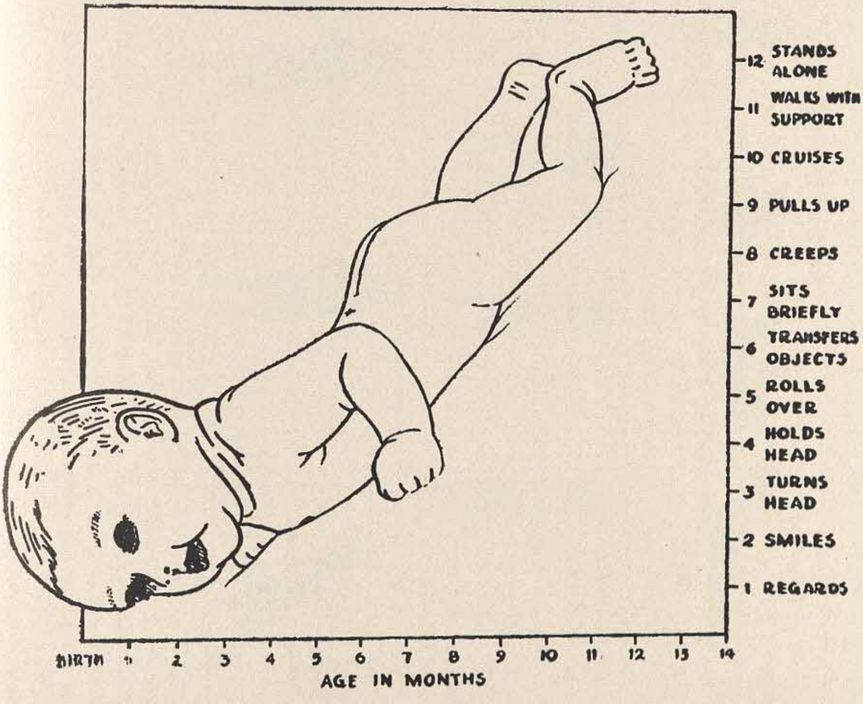

FIGURE 71. In this developmental graph for the first year of life, the infant represents a diagonal on which is plotted the progress of behavior (right) against age (below). The cephalocaudal sequence displayed in the maturation of the infant's behavior is diagrammatically illustrated by the position of the figure. As far as the head is concerned, early acquisition of motor ability for the ingestion of food is common to the whole animal series. Since anencephalic infants display this ability, subcortical parts of the brain are adequate for its management. Reprinted from Aldrich, C. A., and Norval, M. A.: A developmental graph for the first year of life. *J. Pediat.* 29, *304 (1946).*

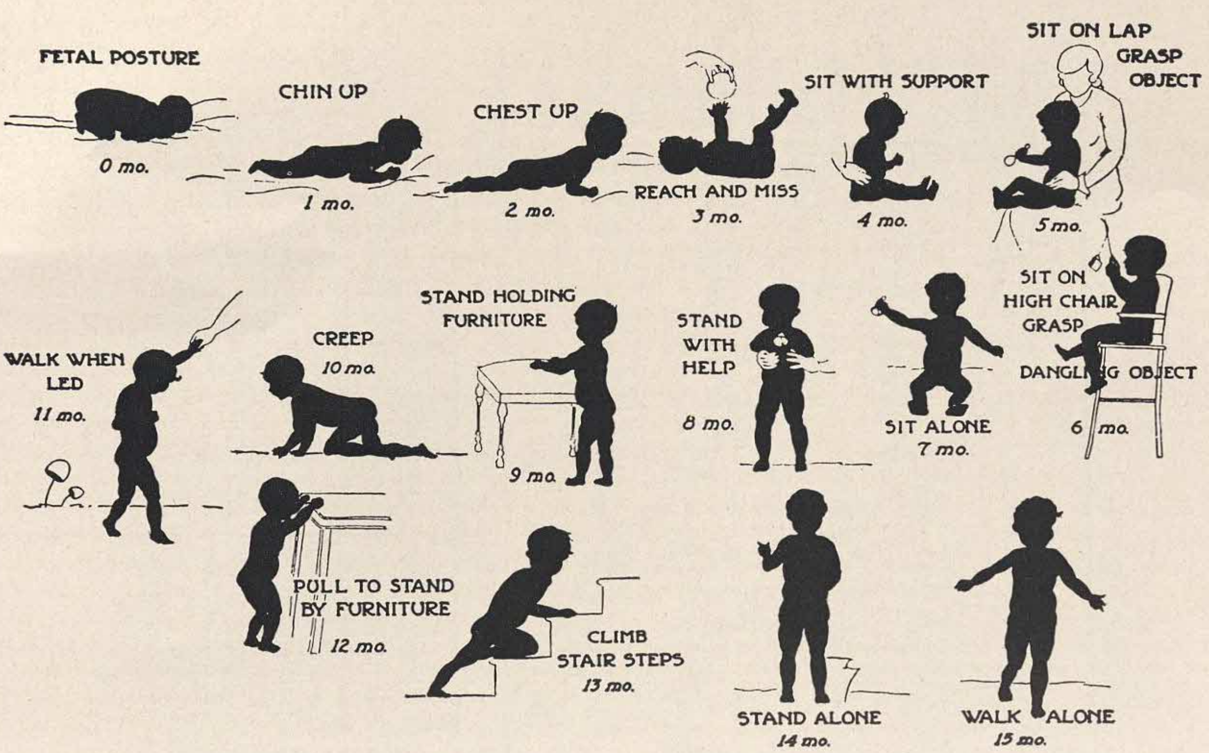

FIGURE 72. A more elaborate presentation of the sequence in which motor capacity develops in the infant shows monthly stages for the first year. Motor capacities of the head and neck are gained first, between 0 and 2 months; those of the arm and hand next, from 3 to 7 months; and those of the lower extremities last, from 8 to 15 months. While reflex-like, food-ingesting activities of the human infant are functional from birth, man differs from all other animals in the great prolongation of development of motor abilities which depend upon cortical function. Reprinted from Shirley, M. M.: *The First Two Years.* Minneapolis, University of Minnesota Press, 1933.

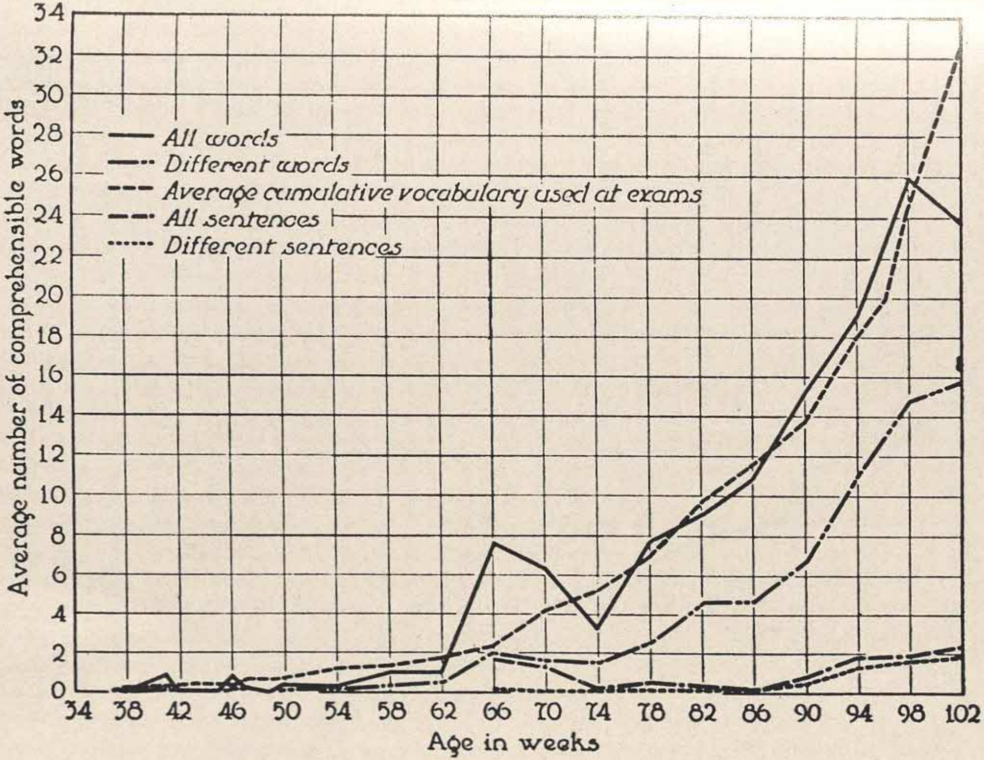

FIGURE 73. Graph showing the number of comprehensible spoken words and sentences recorded at successive psychological examinations between 34 and 102 weeks. Like his food-ingesting abilities, the motor capacities of the oro-pharyngo-laryngeal region, subserving the vocal expression of emotion, are present from birth in the human infant. The much later appearance of spoken words and sentences, between 1 and 2 years of age, is an expression of the delayed maturation of function in cortical associational areas. Obviously, different neural mechanisms subserve these two methods of communication, the latter of which is present only in man. Reprinted from Shirley, M. M.: *The First Two Years*. Minneapolis, University of Minnesota Press, 1933.

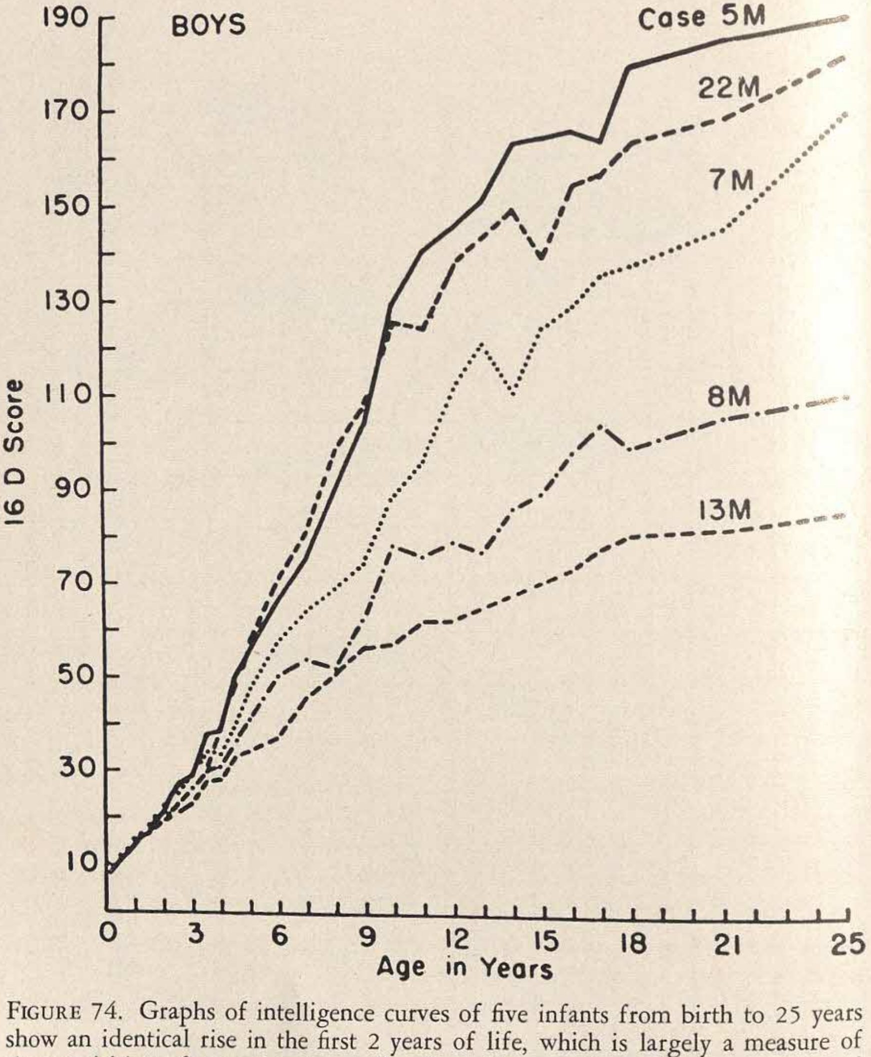

FIGURE 74. Graphs of intelligence curves of five infants from birth to 25 years show an identical rise in the first 2 years of life, which is largely a measure of the acquisition of sensori-motor skills. From the age of 2 to 4 years, speech and language capacities develop, and the subsequent considerable variation in the different individuals is largely a measure of their abilities in the manipulation of symbols. This is to some degree related to the general intellectual factor that most intelligence tests are designed to measure. Reprinted from Bayley, N.: On the growth of intelligence. *Am. Psychol.* **10**, *805 (1955).*

# BIOCHEMICAL MATURATION OF THE CENTRAL NERVOUS SYSTEM*

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*Magoun:* This conference has to do with the maturation of the central nervous system and behavior. We greatly regret the absence of an anthropologist in the program; however, as a poor substitute, a pictorial survey has been prepared of the Evolution of Man's Brain, and is presented as an introduction to the conference. As the program indicates, this meeting will begin with biochemical and physiological maturation, then pass to the maturation of behavior, and conclude with consideration of the maturation of behavior in man.

*Roberts:* The general area which we are called upon to discuss at this conference is a particularly difficult one for the biochemist. A biochemist usually presents empirical contributions at a meeting: the discovery of a new substance, the elucidation of some aspect of an enzymatic reaction or biosynthetic mechanism, the sequence of reactions in a metabolic cycle, the activity of a new hormone, etc. At this conference, the object is to attempt to integrate the findings of biological, chemical, medical, and social sciences in such a way that more meaningful unities become apparent. We are to be concerned with the links between various disciplines in formulating descriptions, possibly explanations, of various phenomena observed as behavior.

*Fremont-Smith:* It seems to me that the great need in science today is not only that it be multiprofessional but that there be a search for new unities, new generalizations. New information is pouring in at a progressively accelerating rate, in all fields, and unless we find these new unities we will be completely inundated by the mass of data. These new concepts must be not only within disciplines but also particularly across disciplines.

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*Roberts:* Since I do not believe there is such a thing as a little bit of honesty, I must say that I believe no great contribution has come from biochemistry which has enlightened the general area of study with which we are concerned. However, there is reason to believe that information being supplied from biochemical fields at an ever increasing rate may be utilized in the future in making such contributions.

To envision the possibilities more clearly, it will, perhaps, be worth while to attempt to place biochemical endeavor in a scheme of current effort in the biological sciences in general. The biologist is concerned with the unique phenomena observable in living organisms and formulates questions about the various classes of these phenomena. In recent years, the application of newly attained precise and sophisticated concepts and techniques of chemistry and physics have enabled the biologist to get some important answers about the substance of living things, how it is made and degraded, and the manner in which it is organized.

As a rough guess, we might estimate that we may now know the structure of about 10 per cent of the chemical substances that are present in living cells. This represents heroic effort and tremendous progress. However, we should not forget that the chemical nature of perhaps 90 per cent of the substances which are present in living cells is, therefore, still unknown. We are just beginning to get some detailed knowledge of how simple molecules like amino acids can be made, degraded, or utilized for various synthetic purposes. We have gained some insight into how the complex molecules, the real bricks and mortar of life like the nucleic acids, polysaccharides, proteins, and the complex lipids, are made. But we are far from knowing all of the details of these processes and know little or nothing of the nature of their regulation within living cells.

With regard to the organization of the chemical substances within cells, the biochemist has taken a cue from the cytologist and has tried to look at the chemistry of isolated nuclei, mitochondria, microsomes, endoplasmic reticulum, etc. We all have seen many papers about a mitochondrial enzyme of one sort or another in brain. A recent paper has shown electron micrographs of the so-called "fractions" that the biochemist usually prepares from brain (55). These appear to be such a mixture that they cannot safely be called anything, and must be described merely in an operational manner. Morphologically well-defined fractions have been prepared from other tissues.

*Abramson:* Dr. Roberts, in saying that 10 per cent of the chemicals are known, what do you mean by "the chemicals"? Do you mean the chemicals after tissues are broken down, or chemicals as they function within the cell?

*Roberts:* I was referring to the chemicals which are obtained after tissues are broken down, and 10 per cent was a rough guess. Until quite recently, extracting the chemicals from dead cells was the closest method available to the chemist for the study of the complex molecules known to be in living cells.

*Abramson:* So these are degradation products. Would you be willing to give us a figure on how much we know of the actual chemical structures as they function within the living cell?

*Roberts:* I would say that is negligible.

*Abramson:* That's the point.

*Leake:* But new techniques are developing, for example, with fluorescent spectroscopy. Other methods have been applied with phase contrast microscopy to the living cell.

*Roberts:* I think Chance's work showing the changes in living cells with rapid spectrophotometric methods is an example of a beginning in that direction (9). However, measuring the reduction of TPN and DPN and changes in the oxidation states of cytochromes is still not telling us much about the actual states of the various enzymes which are performing the reactions. Living cells are highly heterogeneous systems containing thousands of different chemical substances of varying degrees of complexity in physical and chemical interaction with each other.

*Abramson:* But I think there are 150 metal-containing catalysts which are involved, and we certainly know very little of the structure.

*Roberts:* That's right. Neither biochemistry nor any other science, as far as I know, has illumined that side of the question which asks, "How do all of these verifiable observations add up to what is observed in the living cell?"

To date, the greatest proportion of the effort of the biochemist has been devoted to the description of the properties of the chemical entities that can be extracted from *once-living* matter. This approach came directly from the tradition of organic chemistry, which had shown that compounds similar to those found in living things could be made in the laboratory and were susceptible to structural and quantitative analyses.

One of the difficult problems in the study of the chemistry of the nervous system has been the characterization of pure chemical entities from the difficultly analyzable mixtures that brain substance represents. Many studies, indeed, have been made of the various lipid constituents of brains of various species at different times in development. However, only in the recent past have techniques been developed which can lend validity to such studies. In no instance known to me has a complete study been made of the time-course of change of completely defined lipid constituents throughout the period of development of an area of brain in a particular species. To make valid analyses in this field, it is necessary to isolate the various types of lipids quantitatively, so that enrichment of one particular type does not occur during the isolation; and in pure form, so that the analyses for substances which are found in various types of lipids, such as fatty acids, the carbohydrate moieties, organic bases, etc., do not overlap. Because such considerations have not been taken into account in myriad studies performed to date, little weight can be given to their meaning in a quantitative sense in any developmental scheme. Only recently has there appeared a paper in which the cerebrosides of rat brain have been characterized in an adequate manner and the changes in the acid components, long chain $\alpha$-hydroxy fatty acids, with age have been described in the whole brains of rats from 23 to 418 days of age (32). Even this latter elegant study has been performed on whole rat brain, and the extension of this kind of work to different brain areas and to subdivisions which eventually would have to be as small as individual neurons is still considerably in the future.

For the first time, the techniques are becoming available which employ adequate knowledge of the chemistry of these often labile substances. Suitable gas, column, and paper chromatographic techniques, infrared spectrometry, and enzymatic procedures are all being assembled in some laboratories for a big push, and we are waiting with great excitement for the first paper that is going to give a complete lipid analysis of the normal human brain. I think that this will be one of the great landmarks in the biochemistry of brain. Yet it will be only the first step on the road to relating the lipid substances to those properties of the individual neuron and neuronal groups which are concerned with conduction and modulation of nerve impulses, and to the normal and abnormal development of these structures.

*Doty:* What per cent of the brain material is composed of lipids? You would be exceeding your "10 per cent known" figure would you not?

*Roberts:* Yes, the 10 per cent would be exceeded if what I said can be achieved. I think years of work are left, but the goal is in sight.

*Fremont-Smith:* Since this stage is the analytical one, would the next stage be to see how these substances actually function?

*Roberts:* Yes, that's right. The next questions to be answered would be related to how the substances are made and interconverted, the relative rates of turnover, the nature of the association with other cellular constituents, etc.

*Fremont-Smith:* And how these relate to the actual functioning of the brain?

*Roberts:* Before that, one must know whether or not the substance is associated with proteins and polysaccharides. Is it a constituent of the neuronal membrane, or is it in the mitochondria? These questions must be answered before one can begin to relate a specific chemical to function. The proper pursuits for the *chemist* or for the *biochemist*, at the present time, are those related to the study of problems of the nature of those which I mentioned previously, rather than to be concerned with whether cerebrosides, proteins, or ribonucleic acids are related to memory traces. Eventually someone might gain a great insight into this kind of problem. However, the scientist who is interested in the chemistry of the lipids is not going to be concerned with such factors at the moment, but is going to be concerned with the structure and analysis of lipids. His horizons have expanded recently to such an extent that he is able, realistically, to look forward to complete partitions of lipids in various biological materials. This will certainly give the person who is interested in whether or not lipids are concerned with memory a much greater amount of information with which to deal at his level.

*Keller:* This scarcity of information with regard to the lipid is not confined to the brain. It applies to the entire body. We know much more about carbohydrates and proteins than we do about the lipids.

*Roberts:* Yes, in a way. But even studies of polysaccharides, proteins, and ribonucleic acids leave some very important gaps between the chemical observations and any functional interpretations. Sequential studies of changes in polysaccharide, protein, and deoxyribo- and ribonucleic acid contents in brain or in various areas of brain have been performed in a variety of species. But here again, the methodological problems have been to a large extent insurmountable to the present time. It has not been possible, generally, to study individual pure constituents of these complex substances and to evaluate their changes in a quantitative manner that would be meaningful in molecular and functional terms. Even if it were possible at the present moment to follow the change in concentration of a particular protein or ribonucleic acid, for example, in a single cell during the complete course of development, what still could be concluded from such an analysis?

Let us be somewhat more specific. Suppose that we were to be able to follow the change in concentration of a specific transfer ribonucleic acid (77). This is a ribonucleic acid moiety which is involved in the combination with amino acids prior to their incorporation into proteins by the action of microsomes. Presumably, each amino acid has its own transfer RNA. The knowledge of the change in content of one of these would not tell us anything about the major process in which this RNA participates, because we would not know the levels of the other amino acid transfer RNAs, or of the enzymes or cofactors which are involved in the total process of protein synthesis. The number of quantitative determinations which it would be necessary to perform to define the system would be astronomical, and yet even if all the values were obtained by the methods which are available today they could not be synthesized into a description of the operation of protein synthetic mechanisms at any time in a particular neuron.

Let us take another example, that of measuring the activity of a particular enzyme as a function of age. Many studies have been made of changes in enzyme levels in the nervous system occurring as a function of age of the organism and the results have supported the conclusion that major changes occur in enzymatic patterns in the developing brain. Most of the studies were made using the whole brain or cortex. The chemical composition of brain areas obviously reflects the composition of its histological components: astrocytes, neurons, glia, myelin sheath, etc., and the relative amounts of each of these elements present in the structure analyzed. Analysis of the whole brain does not distinguish changes in one category from those in another. An elegant study was performed recently in which four enzymes were examined in individual cortical layers using quantitative microchemical procedures in newborn, 10-day-old, and adult rats (39). Determinations were made of lactic, malic, glutamic, and glucose-6-phosphate dehydrogenase activities. Delicate ultramicro methods were used. It was concluded that during maturation nonmyelinated cortical layers increase greatly in ability to utilize glutamate and to a lesser extent in capacity for oxidation of glucose through the citric acid cycle, and that at the same time there probably is little change in glycolysis or in direct glucose oxidation. These are extremely valuable data to have, and it is this sort of chemical information which eventually may be correlated with some physiological properties of the cortical layers studied. However, for the present, it is impossible to relate these observations to specific electrophysiological or behavioral measurements which might be made in the same animals.

Enzyme measurements usually are made in homogenates fortified to elicit the maximal potential activity of which the system is capable. Otherwise, with our present methodology, quantification is extremely difficult, if not impossible. Whether or not measurements performed in this manner, in which tissue structure has been destroyed and permeability barriers have been altered, reflect activities which are occurring in neurons in particular cerebral areas at a particular time is a question which often must remain unanswered. There is still a tremendous number of quantitative determinations that must be performed, many substances and biochemical relationships to be discovered, and many studies to be conducted with little hope of obtaining information which may be of immediate functional importance.

One of the important contributions to our thinking about problems of development may be the recent work of Pardee, Jacob, and Monod (52), who have described experiments with certain mutants of *Escherichia coli* which have indicated that there are genes which may control the formation of substances that act as repressors of formation of enzymes. There are two classes of enzymes, inducible (or adaptive) and constitutive. The inducible enzymes fluctuate in response to environmental changes in microorganisms and animals. When substrate for an inducible enzyme in bacteria is present in the medium (or a substance which can mimic the effect of substrate), the plot of enzyme activity versus time gives a curve that rises rapidly from an undetectable level and exhibits a sigmoidal shape. Constitutive enzymes are not influenced in this manner by substrate and tend to remain relatively constant under widely varying conditions [see Knox, *et al.* (37) for references to work with animals]. The work of Pardee, *et al.* (52) suggests that at least in *E. coli* the constitutive state results from the loss of the capacity to synthesize active repressor. Szilard (81,82) gave an extension of these ideas and possible applications to protein synthesis in animal cells. Determinations of sequential changes in enzyme activities in different tissues (including nervous system) of various species have revealed that a number of enzymes exhibit a sigmoidal temporal increase during development similar to that found for inducible enzymes in bacteria (24,37,50,75). Perhaps enzyme increases during differentiation and development might be attributable, at least in some instances, to a reduction in the effective concentrations of repressors of the formation of the enzymes. Although this concept presents myriad opportunities for conjecture, it is difficult to see at present how critical experiments could be performed to determine whether such mechanisms are operative in animal material.

Suppose that it has been shown that an enzyme increases during development in a sigmoidal fashion in a tissue, group of cells, or in an individual cell. What does this really mean? If the enzyme is associated with mitochondria, it must be determined whether the mitochondrial population is changing or whether there are only more mitochondria per cell. For every enzyme, this kind of problem must be settled. Then the more difficult problems arise in trying to relate the enzyme measurements to morphogenesis and function.

In studying enzyme activities, a chemist often makes a homogenate; first, he wrecks all the structures, breaks down many of the diffusion barriers with a good homogenizer which is built especially for this purpose, and then he loads the system with substrates and cofactors and adjusts the pH so that the only factor which limits the reaction rate is the enzyme concentration. Only then do the results have validity from a quantitative point of view.

How do these measurements refer to what is present in the cell? How does this tell you about the barriers between the various cellular compartments which we know must exist? How do we know whether or not an enzyme in the cell is in association with the optimal amount of substrate which will maintain its activity at a maximum at all times. We do not know these things, but, still, this is the only way at the present time that we can measure the activity of most enzymes to obtain technically valid results. Otherwise, we would be in a *totally* uninterpretable area. This way, at least we can make some inferences which we can check back and forth by independent methods; for example, we can inject an isotopically labeled substrate, determine how rapidly it is converted to a product, and compare the result with what is obtained when the tissue is taken out; we can then homogenize the tissue and perform measurements of the activity of the enzyme which catalyzes the particular transformation.

*Sokolov:* Dr. Roberts, what aspect of maturation is reflected in biochemical processes and in what form? What is your concept of biochemical maturation?

*Roberts:* As I interpret it, it would be something like the following: Biochemical maturation of the nervous system consists of the changes in time of those properties which are germane to the main specialized function of the nerve cell, which is generation and conduction of nerve impulses. I would not interpret a study of biochemical maturation as meaning an attempt at analysis of all chemical variables that change as a function of age. Rather, it would be an effort to analyze from all points of view those factors which might be sufficiently important to be rate-limiting in the final functional participation of neurons in the activity of the nervous system as a unit.

*Leake:* And you mean both ontogenetically and phylogenetically?

*Roberts:* As I was talking, I was thinking of changes taking place in a particular neuron, in a particular area. I was trying to think in those specific terms rather than in broader terms. What I was saying previously was in the way of an introduction and qualification of the participation of the biochemist in the chemical study of the brain and I was pointing out that there are severe limitations at the moment, technically and philosophically, in using biochemical findings to explain the phenomena with which we are concerned at this conference. The biochemical information obtained to date is still relatively unintegrated into the total scheme of things.

There are certain *new* landmarks in biochemistry of the brain which are very important and, although they have not as yet given us the type of information we want, they are leading the way. One is the approach by Lowry (45), Hydén (29), Pope (60), and others, in which a study is being made of relatively small cell groups and individual neurons. Some idea about maximal functional capacity is being derived. This type of endeavor is attempting to integrate cytology, histology, and biochemistry. The approach of Flexner and coworkers is even broader (19). They are making an extended effort to add electrophysiological and behavioral observations to those made employing other disciplines. None of the approaches has yet given information that could be even remotely related to the level at which this conference is pegged, *i.e.*, behavior of human beings in a social environment. However, they constitute important beginnings and serve to indicate that there are workers in these areas who understand the technical difficulties and are prepared to brave them.

I might say that it takes some courage to enter an area like this, because a biochemist can always stay safely in his own backyard, crystallize new enzymes, study their kinetics and active centers, and earn the approval of his colleagues. As soon as he steps out into an attempt to explain some phenomenon of life, he is severely criticized. I have felt this even in the few physiologically or pharmacologically oriented studies in which we have been engaged. However, I think the only way to progress is to overcome fears and insecurities and to try to answer the criticisms.

The contact of a nerve cell with an end organ or with other nerve cells may alter the properties of that nerve cell (80). There is probably some sort of exchange of material or information. How could chemists even begin to approach this kind of study? Isn't it of primary importance to know how, in its development, an exchange of chemical information takes place between a particular nerve cell and other cells in a way that causes this nerve cell to take on very specific properties which make it different in many respects from its neighbors? This is a tremendously important and interesting field to study, but, as far as I can see, the chemist has almost no methodological entry into this problem at the moment.

*Purpura:* There are a number of examples that can be cited to illustrate how the properties of effector cells can be radically altered by factors operating via their innervation. One of the most interesting problems that has recently been a subject of renewed investigation concerns the remarkable similarity in properties of fetal mammalian muscle and chronically denervated mature mammalian muscle. Fetal skeletal muscle fibers (14), like chronically denervated mammalian muscle fibers (2), are sensitive to iontophoretically applied acetylcholine over their whole surface. The membrane properties of fetal muscle begin to change shortly after birth in the rat, and by the end of the second week, chemosensitivity is restricted to the end-plate region as in mature animals.

*Bodian:* You mean fetal or preinnervated muscle?

*Purpura:* I don't believe that the global chemosensitivity of fetal skeletal muscle membrane is due to the lack of motor innervation. We recently became interested in this problem through some observations on the effects of intravenous succinylcholine in the newborn cat (63). It has long been known that acetylcholine induces skeletal muscle contractures in fetal and newborn mammals. We observed long-persisting generalized skeletal muscle contractures in the newborn cat on injecting succinylcholine. The typical effects of succinylcholine, *i.e.*, generalized fibrillation, then flaccid paralysis, were not observed in kittens until after the 10th to 14th postnatal day. This raised the question as to whether the effects of succinylcholine in the neonatal cat were attributable to a deficiency in motor innervation. To answer this, we did some electromyograms in newborn cats and observed changes in the EMG following muscle stretch and after eliciting a variety of reflexes. Our data indicate that the skeletal muscles of the newborn cat are capable of participating in a wide variety of reflex activities. No deficit in innervation could be detected, at least physiologically.

The fact that functionally innervated mammalian skeletal muscle fibers in the newborn mammal are globally chemosensitive to acetylcholine and acetylcholine-like compounds such as succinylcholine suggests that during the latter phases of ontogenesis, motor axons exert some effect on muscle fibers apart from their ability to inject acetylcholine at the end-plate region. This effect, whatever it may be, becomes fully established by the second postnatal week, and apparently it is lost several days after interruption of motor axons in the mature animals. Recent studies by Axelsson and Thesleff (2) reveal that the chronically denervated mammalian skeletal muscle fibers are not more sensitive to acetylcholine injected from the end-plate region, but rather that the muscle fiber membrane away from the end-plate region has become chemosensitive. Chronically denervated skeletal muscle fibers are electrically excitable as well as chemically excitable (2), thus suggesting that in the denervated state the muscle fiber membrane has not undergone a homogeneous change toward chemosensitivity, but rather that some membrane sites acquire chemoreceptor properties.

*Bodian:* This is similar to the sensitization of denervated ganglion cells?

*Purpura:* The increased sensitivity of chronically denervated mammalian skeletal muscle to acetylcholine was demonstrated many years ago. The studies of Axelsson and Thesleff (2) have permitted a more detailed account of this phenomenon. During ontogenesis, muscle fibers, like those in chronically denervated muscle, are sensitive to the depolarizing action of acetylcholine over their whole surface, and this sensitivity is associated with a high myosin-cholinesterase and low myosin adenosine triphosphatase activity as has been shown by Varga, *et al.* (85). Our own studies indicate that the sensitivity of skeletal muscles to succinylcholine in the newborn cat is not due to a detectable deficiency in their motor innervation. We have concluded from this that the changes in the properties of mammalian skeletal muscle occurring during the later phases of ontogenesis are brought about by some influence exerted by motor axons apart from their ability to discharge acetylcholine. When this influence is eliminated by interruption of motor axons, it appears that mature skeletal muscle again displays characteristics which it possessed in the fetal animal.

*Livingston:* If you increase the traffic of nerve impulses in the fetus or in the newborn, could you, locally, in those muscle areas, create a change toward the adult type earlier than would occur at the usual maturation time?

*Purpura:* I don't know whether that experiment has ever been performed or not. Of course, "fetal" muscle responds differently to tetanization than does mature muscle. This has been known for many years.

With respect to the influence of the central nervous system on the changing properties of skeletal muscle during ontogenesis, I am reminded of a most interesting report dealing with the augmentation of the acetylcholine-contracture of fetal muscle by cerebellar stimulation. It was in the series of translations from the Russian literature distributed prior to this meeting. The experiments reported by Khudorozheva (31) consisted in measuring the magnitude of a standard acetylcholine-contracture of fetal rabbit gastrocnemius muscle before and after cerebellar stimulation. From the published records, it appears that cerebellar stimulation produced approximately a 75 to 100 per cent increase in the magnitude of the acetylcholine-contracture. Khudorozheva inferred from this that some humoral agent released from the cerebellum was responsible for potentiating the action of acetylcholine on the fetal muscle. These effects of cerebellar stimulation were not observed after the sixth to tenth postnatal day.

*Magoun:* Is it possible that the intrafusal fibers, the muscle fibers within a muscle spindle, preserve this embryonic capacity into adulthood? The reason I ask that is that succinylcholine causes a barrage of afferent firing from a muscle spindle, the basis of which has been obscure. Might it have an explanation in pharmacologically induced contraction of the intrafusal muscle fiber and stretch of the afferent ending around its center?

*Purpura:* Recently, Eyzaguirre (18) has shown that propagated action potentials may be recorded from single mammalian intrafusal fibers following fusimotor nerve stimulation. From this, it is concluded that intrafusal fibers resemble extrafusal fibers and not the "slow" muscle fibers of lower vertebrates. Eyzaguirre also makes reference to the studies of Cuajunco (11), who showed that intrafusal fibers develop from the same elements which eventually produce extrafusal fibers. In the newborn animal, the structure of intrafusal and extrafusal fibers is apparently similar except that intrafusal fibers appear more immature. Dr. Magoun has posed a very interesting question as to whether the barrage of activity produced in muscle spindles by succinylcholine may be related to some residual embryonic features of the intrafusal fibers. I don't think we have enough data to explain the action of succinylcholine on muscle spindles (25). Physostigmine is known to produce repetitive intrafusal discharges (18), and probably succinylcholine acts similarly.

*Bodian:* What you said reminded me of Flexner's pioneering work on the maturation of the cortex (20). As you recall, he found that there was a relationship between the oxidative enzyme development, cytological maturation, and origin of electrical phenomena. The increase of cytochrome oxidase activity which was found at this critical stage of embryonic development was the reverse of the change which we found to occur in a motor neuron when the axon is cut. This is followed by a decrease of cytochrome oxidase activity and related enzymatic activity, and, at the same time, the micromorphology of the cell changes to a form which resembles that in the embryo. My interpretation of Flexner's study is that he was really studying events related to the developing role of the axon, as was demonstrated in reverse in the adult, by experiments on the differentiated axon (7). In spite of this promising start, there has been very little study of the maturation of the cortex, with the idea of tying in more complex relationships at the microscopic level with events at the electrophysiological and behavioral levels (28).

*Windle:* There is some work in progress now along that line. Schadé (73) in Holland has been doing some very interesting work on the early maturation of the dendritic tree in the cerebral cortex. Some of his findings integrate quite well with Flexner's studies in the guinea pig (54).

*Bridger:* With respect to behavioral phenomena, Kasatkin (30) reported that both full-term and premature babies develop their first conditioned responses 3 weeks after birth, even though their age from time of conception may differ by 2 months. It seems as if some sort of post-natal experience is a determining condition for the maturation of whatever is involved in the ability to form conditioned responses.

In Professor Luria's (46) study of twins who had not developed speech until the age of 5½, he reports that once they were separated they were able to acquire adequate language ability in 3 or 4 months. They also developed a capacity for conceptual thinking approximately equal to their peers in the same short period of time. It would appear as though a biological or biosocial maturation process had in some way been going on during their life independent of cognitive development. It was this maturation which then enabled them to catch up so quickly with their peers in the area of cognitive functioning.

*Roberts:* I am glad that Dr. Purpura brought up the problem of the membrane. This is one that has really concerned me, as a biochemist. We would like to find out whether the glutamic acid decarboxylase, the enzyme which forms GABA, is on or close to the membranes of the dendrites and nerve cell bodies. There is at present no histochemical procedure for the visualization of the enzyme, nor is the development of one in sight. The question is, therefore, how, with any known techniques, could we find out if the enzyme is associated with neuronal membranes? No satisfactory technical suggestion has come forth, even though we have called and spoken to many individuals whom we know to have done histochemical, histological, and cytological work on the nervous system. None of the stains and techniques of visualization which are possible on sections, where structures are well oriented, would be at all suitable for application to a pellet spun down in a centrifuge tube after homogenization of nerve tissue. Thus, a problem which is so pertinent for the nerve cell—to determine whether a certain enzyme which may be important in the reactivity of the membrane is actually present on the membrane—has at this moment no apparent technical solution.

I turn your attention now to the area with which I have been directly concerned, the changes in some of the factors concerned with the metabolism of GABA in the developing brain. Chemical and physiological findings related to this area of activity have been summarized elsewhere by a number of workers in this field (66).

After the biochemist became intrigued with the unique presence of GABA in the central nervous system, the physiologist and pharmacologist obtained data which indicated that this substance, directly or indirectly, was related to processes which were called inhibition in various neurophysiological test systems. By alteration of the levels of GABA, either exogenously or endogenously, the measurements of properties related to inhibition were changed.

The physiological effects of GABA seem to be related to effects on the ionic movement and are rather complex in many ways, as measured by the neurophysiologist. I will leave a discussion of those aspects to Dr. Purpura, who has been as complex as anyone in terms of things that he has derived with regard to the physiological effects of GABA. This doesn't mean that he hasn't shed any light on the subject. I mean, rather, that it is difficult and complex for a biochemist to understand the tracings which he and others have published.

Because of the intense experimental activity and several fortunate coincidences, the work on GABA is now in a stage at which there is some hope of eventually getting unifying generalizations with regard to inhibitory phenomena, neuronal activity, membrane properties, and biochemical processes. We may have an example of what Dr. Fremont-Smith has been mentioning, a situation in which it is not a requisite to know all of the details in a particular scientific area before achieving some unifying generalization.

In the most direct studies performed to date, it was found that low concentrations of GABA had effects on the crayfish stretch receptor which were remarkably similar to those found on the stimulation of the inhibitory nerve (38). GABA concentrations one thousand times stronger than those blocking afferent discharge did not block conduction in the sensory axons. GABA action, therefore, appears to be confined to the dendrites and cell body. It is now believed that some substance other than GABA is the naturally occurring inhibitor in the crayfish system (22). However, since GABA is found in large amounts in the central nervous system of all species studied, it may be that in those sites where it exists it exerts an action on neurons similar, at least in some respects, to that in the crayfish stretch receptor test system.

In what follows I will try to explain some of the chemical facts known about the GABA system. The scheme in Figure 75 outlines the known reactions of GABA in the central nervous system. GABA is formed in brain from L-glutamic acid by the action of L-glutamic acid decarboxylase (GAD), an enzyme found to date in mammalian organisms only in the central nervous system, chiefly in the gray matter. At the present time, of the enzymes which have been studied in the brain, I think that this is the only one which has such a unique distribution, not being found in any other tissue. It is possible that it will be detected elsewhere, but in the tissues which we have examined by the methods which we have employed, it has not been found anywhere other than in the central nervous system.

GABA-α-keto-glutarate transaminase (GABA-T), an enzyme found in brain as well as in other tissues and in microorganisms, catalyzes the reversible transamination of GABA with α-keto-glutarate. Brain also contains a dehydrogenase which catalyzes the rapid oxidation of succinic semialdehyde, the product of transamination of GABA, to succinic acid, which in turn can be oxidized through the reactions of the tricarboxylic acid cycle. The end result of the existence of these pathways in the central nervous system is that there is a possibility of a shunt (or a bypass) around the α-keto-glutaric acid oxidase, one of the enzyme systems of the tricarboxylic acid cycle. No valid method has been devised yet to get a realistic value for the contribution of this bypass toward the energy metabolism of brain in intact animals. However, an estimate of approximately 40 per cent was made for the contribution of the GABA shunt to the oxidative metabolism of brain cortex slices (48). From simultaneously performed histological and chemical

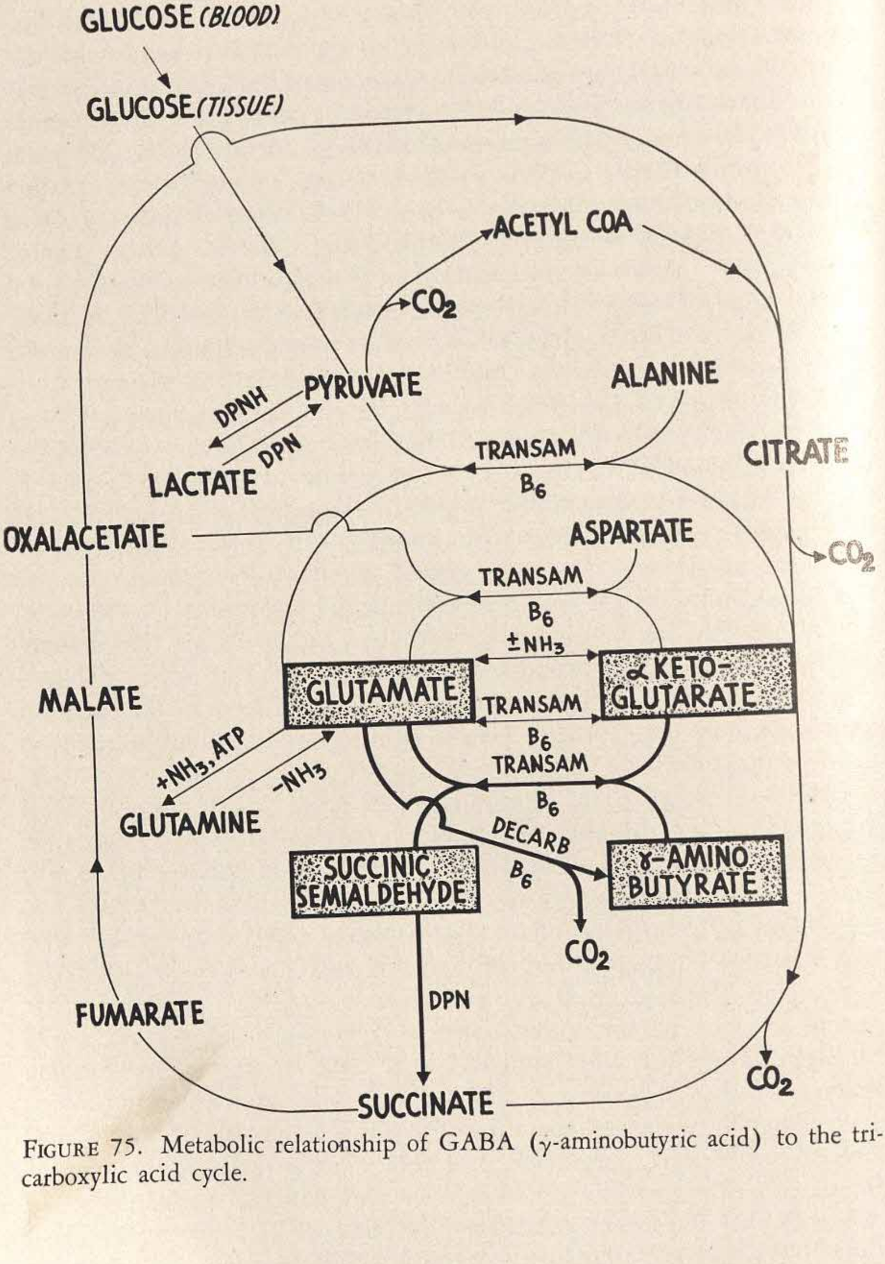

FIGURE 75. Metabolic relationship of GABA (γ-aminobutyric acid) to the tricarboxylic acid cycle.

studies carried out to date, it has not been possible to correlate exactly the activity of the GABA system with particular types of neurons or neuronal processes. As a result of the operation of the above described metabolic system, there are relatively large amounts of GABA present in various structures in the brain and spinal cord.

The results from both invertebrate and vertebrate test systems suggest that the probable common mode of action of GABA is to cause an increase in the membrane conductance related to an increase in permeability to chloride and/or potassium. Perhaps the simplest way for a chemist to look at the inhibitory effect is to consider that a greater amount of a given type of stimulation would be required to elicit the same response from a given neuronal element when that element has a higher level of GABA than when there is less, provided that the balance of other excitatory and inhibitory factors remains the same.

Of particularly great physiological importance was the finding that both GAD and GABA-T require pyridoxal phosphate, a form of vitamin $B_6$, as a coenzyme. The activity of both of these enzymes depends on the binding of the coenzyme to the enzyme protein and on the presence of a free aldehyde group on the coenzyme. The experiments which have been performed to date suggest that the protein of GAD has a much lower affinity for the coenzyme than the protein of GABA-T. Of the various tissues examined, brain is the richest source of pyridoxal kinase, the enzyme which makes the coenzyme from pyridoxal and adenosine triphosphate (47,68). A number of results have suggested that there might be some relationship between the seizures found in almost all cases of vitamin $B_6$ deficiency in animals and man and the impaired operation of the GABA system. But this is a correlation and not necessarily an established causal relationship at the moment. Great caution must be exercised in reaching any final conclusions in this matter, since pyridoxal phosphate is a coenzyme for many enzymatic reactions, some of which are involved in the biosynthesis of physiologically active substances such as serotonin and epinephrine. Therefore, a deficiency of vitamin $B_6$, whether induced by dietary or chemical methods, might produce very complicated imbalances in normally occurring inhibitory and excitatory factors in different areas of brain and spinal cord.

*Abramson:* Dr. Roberts, would you expand on the ionic mobility just a bit further? It specifically comes into some of the work I am doing. Is this only sodium or potassium, or would you include calcium?

*Roberts:* The only cation which seems to be affected is potassium. Potassium conductance seems to be involved particularly in the invertebrate system, at least in the crayfish stretch receptor, while the conductance to chloride appears to be most greatly influenced in the mammalian systems.

It is most important to emphasize that although GAD is a vitamin $B_6$-requiring enzyme system, there are shown in Figure 75 six reactions which involve a vitamin $B_6$ coenzyme, and there are probably as many as twenty enzymes in the various metabolic systems operating in a neuron or in any cell which requires pyridoxal phosphate. The apoenzymes of all of such enzymes, no doubt, have differing relative affinities for the coenzyme. When a gross phenomenon like a seizure is seen in an animal in vitamin $B_6$ deficiency or after treatment with a vitamin $B_6$ antimetabolite, all we can say is that it is correlated with a decrease in activity of one or another of these enzyme systems. But all of them cannot be evaluated simultaneously, nor can a change in the total balance of products and substrates be measured. It must be realized that the degree of activity in the brain or in any element in the central nervous system is the result of a multiple interaction between the inhibitory and excitatory factors. In the case of the GABA system, however, we may have a handle on one of the possibly important inhibitory influences in the nervous system, and so have an opportunity of shifting the total balance of neuronal reactivity by altering levels of the various components.

*Fremont-Smith:* How early in the embryo is this system evident?

*Roberts:* I will show the results bearing on that point subsequently. Figure 76 shows paper chromatograms made of extracts of brains of eight individual mice of the Swiss strain of both sexes averaging approximately 17.5 gm. in weight. I don't know if you are familiar with this biochemical Rorschach. Extracts corresponding to a given fresh weight of tissue are placed on a piece of filter paper and the constituents are separated by allowing a suitable solvent to flow down the paper in one direction, and then another solvent is allowed to move at 90 degrees to the first solvent. After chromatography, the sheets are sprayed with ninhydrin to show amino acids and other constituents with amino groups. On looking at this pattern, one sees a remarkable constancy of the distribution of the ninhydrin-reactive constituents from one animal to another. Work in our laboratory with tissues from man, dog, cat, rat, mouse, rabbit, chicken, alligator, snake, turtle, frog, salamander, and a large variety of marine organisms has shown that in each species at a particular stage of development each normal tissue, including every type of blood cell, has a distribution of free or loosely bound amino acids which is characteristic for a particular species. Remarkable and

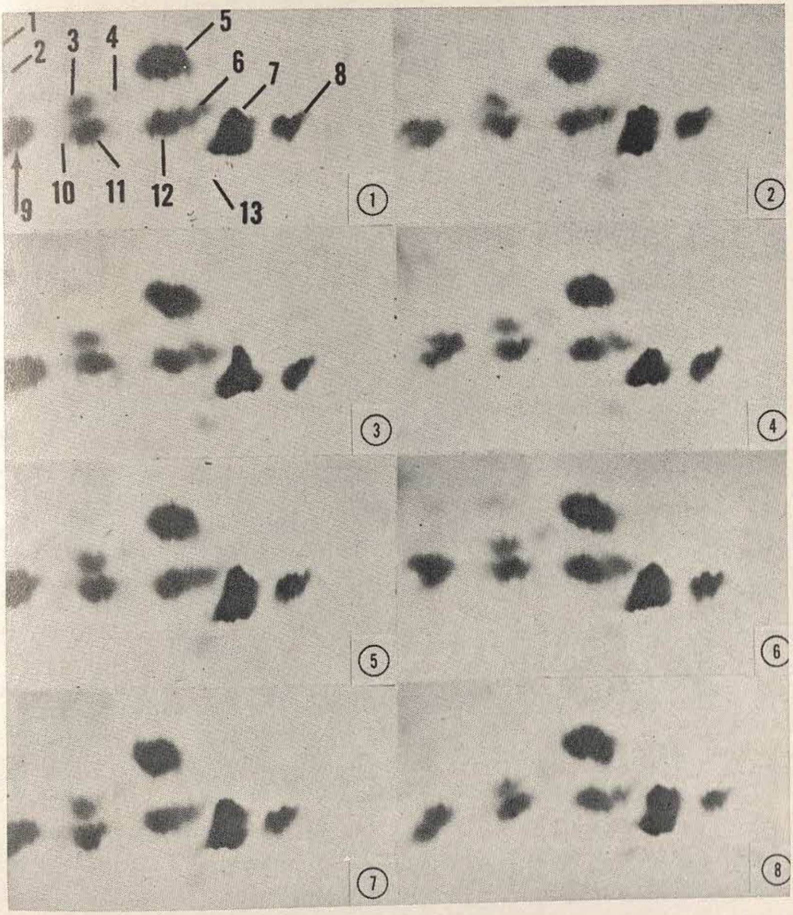

FIGURE 76. Paper chromatograms showing constancy of patterns of free amino acids in extracts of brains (37.5 mg.) of eight Swiss mice. Descending two-dimensional chromatography was performed in water-saturated phenol followed by water-saturated lutidine. 1 = leucine and isoleucine, 2 = valine, 3 = alanine, 4 = threonine, 5 = taurine, 6 = serine, 7 = glutamic acid, 8 = aspartic acid, 9 = GABA, 10 = glycerylphosphorylethanolamine, 11 = glutamine, 12 = glycine, 13 = ethanolaminephosphoric acid.

characteristic differences are found from one area of the nervous system to another. The previous results were on whole brain. For a more specific picture, Figure 77 shows the chromatograms obtained from different parts of the rat brain. These results show clearly that different parts of the brain, grossly dissected, have different patterns

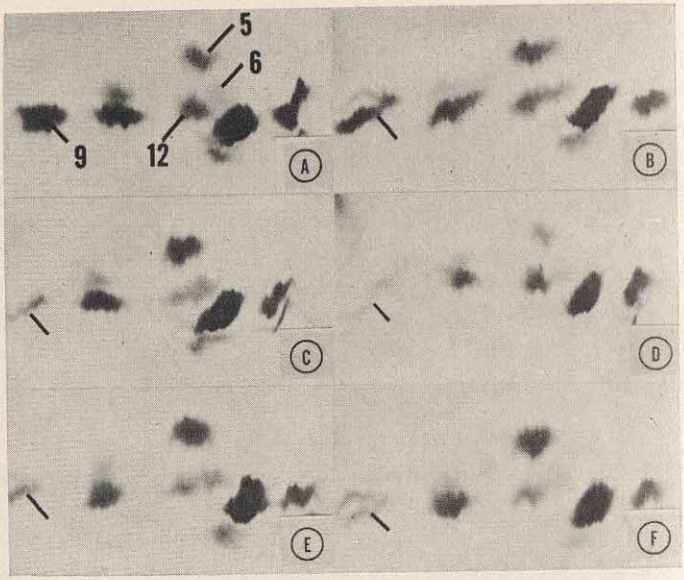

FIGURE 77. Paper chromatograms of extracts obtained from 20 mg. of original fresh weight of different areas of rat brain: (*A*) corpora quadrigemina, (*B*) diencephalon, (*C*) cerebral hemispheres, (*D*) pons and medulla, (*E*) cortex, and (*F*) cerebellum. On chromatograms (*B*) to (*F*), the lines point to GABA. 5 = taurine, 6 = serine, 9 = GABA, 12 = glycine. Reprinted, by permission, from Roberts, E.: Free amino acids of nervous tissue. Some aspects of metabolism of gamma-aminobutyric acid. *Inhibition in the Nervous System and γ-aminobutyric Acid*. E. Roberts, Ed., Oxford, Pergamon Press, 1960 (p. 144).

and from previous work would suggest that every cell type, perhaps every individual neuron, may have its own pattern of these constituents.

By free amino acids, we mean those which are easily extractable. We generally extract freshly dissected tissue with 80 per cent alcohol so that protein is not broken down. Figure 77 shows a great variation of GABA level from one area to another. All ninhydrin-reactive constituents other than GABA also were found in chromatograms of protein-free extracts of other tissues. Many of these chromatograms indicate that GABA shows a greater extent of variation than any other constituent from one area of brain to another.

Electrophysiological measurements of various parameters of excitability made in different parts of cat brain showed no relation to exist between the measurements and the absolute GABA levels (5). Virtually identical levels of GABA were found in areas of cat brain cortex which showed a three-fold variation in seizure susceptibility. A higher level of GABA than was found in these cortical areas was found in the hippocampus, which has an exceptionally low seizure threshold and requires only the mechanical stimulation of exploring with the electrodes to fire convulsive afterdischarges. Actually, one would not expect there to be a simple and direct relation between seizure susceptibility and the level of GABA normally found in a particular area, since the total tone in an area of the central nervous system, of which seizure susceptibility is only one criterion, is a result of a balance of excitatory and inhibitory factors. However, it appears that the GABA system may be of sufficient importance in such a balance so that increases or decreases, respectively, of GABA in a particular cerebral area have been closely correlated with increases or decreases in seizure threshold of that area in many experiments. Certainly at this point one cannot take a unitarian point of view. GABA and the GABA system are one of many factors which are involved. At the moment, it gives us experimental opportunities, because this system can be manipulated in such a way as to swing the balance for increased or decreased sensitivities to stimulation, provided many other variables are not changed by experimental procedure. I hope that this qualifies my point of view sufficiently.

GABA is present in large amounts in the cerebral cortex of the dog (Figure 78) (*A*), but is not detectable in extracts of brachial plexus (*B*) or of optic nerve (*C*). The cortex contains high concentrations of all of the detectable constituents per unit fresh weight of tissue. Increasing the quantities of extract examined from brachial plexus or optic nerve still did not reveal the presence of any detectable amounts of GABA. Similarly, GABA has been detected in brain and spinal cord, but not in sciatic nerve of rabbit (69). The illustration also shows the patterns of free amino acids found in the extracts of whole brain of Pacific mackerel (*D*), alligator (*E*), and Australian opossum (*F*). These results demonstrate the wide variation of various constituents found in extracts of whole brain of various species. Only GABA, glutamic acid, and glutamine were found in large amounts in all of the species, marked variations being observed in the content of the other constituents from one species to another.

We can now get into the developmental features of the GABA system. In all species studied to date, which include the mouse, chick, bullfrog, and rabbit, there was found to be a progressive increase in the content of GABA during development. This was not the case for any of the other constituents detected on chromatograms of the extracts of the whole brain in these species. Figure 79 shows a replot of previously published data on the changes with age in GAD and GABA levels of

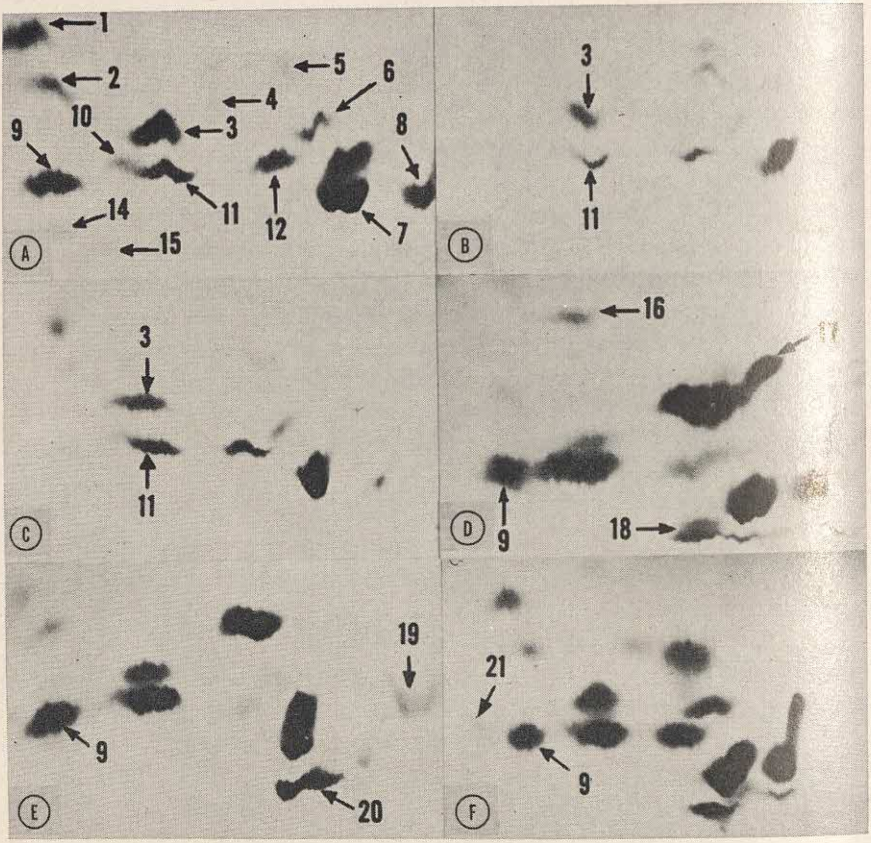

FIGURE 78. Chromatograms of extracts (75 mg.) of dog cerebral cortex (*A*), brachial plexus (*B*), and optic nerve (*C*). Amino acids in extracts of brain of Pacific mackerel (*D*), alligator (*E*), and Australian opossum (*F*). Identification of the spots is the same as in Figure 76. Additional spots are: 14 = arginine, 15 = lysine, 16 = tyrosine, 17 = unidentified, 18 = unidentified, 19 = glutathione, 20 = phosphodiester of ethanolamine and L-serine (found chiefly in reptiles), 21 = proline. Reprinted, by permission, from Roberts E., Lowe, I. P., Guth, L., and Jelinek, B.: Distribution of $\gamma$-aminobutyric acid and other amino acids in nervous tissue of various species. *J. Exper. Zool.* **138,** *313-328 (1958).*

whole mouse brain (70). Up to 5 days after birth, the rate of increase of GABA content was approximately equal to that of GAD activity. From 5 to 20 days, the rate of increase of GAD activity was much greater than that of the increase in the concentration of GABA. Similar results have been found in some parts of chick embryo brain (76) and in an area of rabbit cerebral cortex (Figure 80) (6). These findings suggest that the rate of turnover of GABA might be increasing much

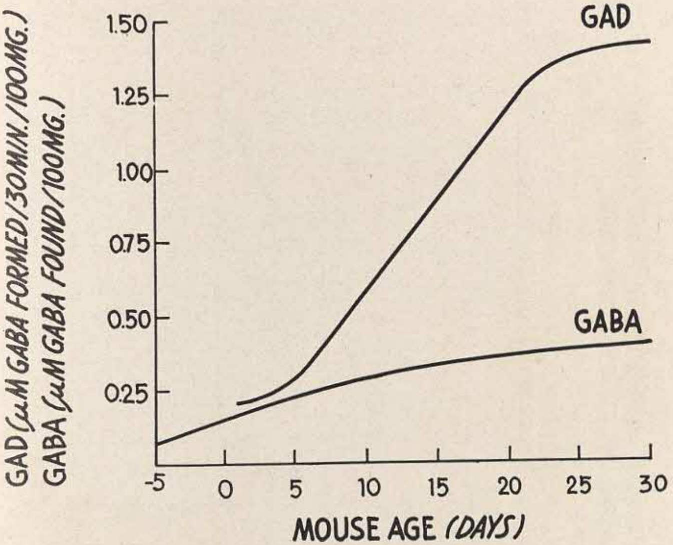

FIGURE 79. Changes with age in glutamic acid decarboxylase activity (GAD) and GABA levels of whole mouse brain. Reprinted, by permission, from Roberts, E., Harman, P. J., and Frankel, S.: γ-Aminobutyric acid content and glutamic decarboxylase activity in developing mouse brain. *Proc. Soc. Exper. Biol. and Med.* 78, *799-803 (1951).*

more than the actual amount of the substance itself during this period. Such an increased turnover could be related to an increasingly important participation of the GABA system in oxidative cerebral metabolism. These inferences are susceptible to test with isotopes in the intact embryos, and we are proceeding in this direction.

*Leake:* You are assuming in each instance that the amount of $B_6$ is constant?

*Roberts:* No, $B_6$ is put into the assay system in tremendous excess. Of course, if there were no vitamin $B_6$ in these brains during periods of development which we studied, there would be no enzyme activity going on, even though the enzyme proteins might be present. However, there is no other way at present of conducting a measurement of the enzyme activities except by putting in sufficient pyridoxal phosphate so that the apoenzymes are completely saturated.

GABA was first barely detectable in extracts of whole brain of the chick embryo on the fourth day of incubation, increasing in quantity with the age of the embryo (71). The development of new and sensitive analytical techniques for GABA, GAD, and GABA-T now has

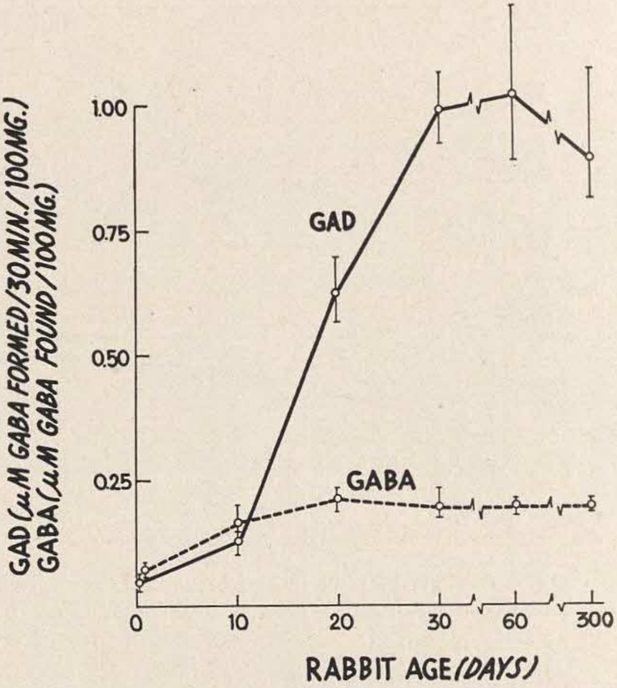

FIGURE 80. Changes with age in glutamic acid decarboxylase activity (GAD) and GABA levels in area 2-3 of the developing rabbit brain cortex. Reprinted, by permission, from Baxter, C. F., Schadé, J. P., and Roberts, E.: Maturational changes in cerebral cortex. II. Levels of glutamic acid decarboxylase, gamma-aminobutyric acid and some related amino acids. *Inhibition of the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 214).

made it feasible to determine the time course of increase of these variables in a single area of brain, the optic tectum, in the chick during embryonic development, and after hatching. The optic tectum was chosen for analysis because a preliminary survey had shown it to have the highest level of GABA in the chick embryo brain and because it furnished a well defined, relatively large structure early in development which is of considerable functional importance in the activity of the avian central nervous system. The chromatograms of the extracts of the optic tectum at various ages (Figure 81) show that a progressive increase occurs in GABA levels and that no other ninhydrin-reactive constituent increases in a similar manner. Ethanolamine phosphate shows a decrease with age. In Figure 82 are shown the results of quantitative measurements performed in collaboration with Sisken and Sano,

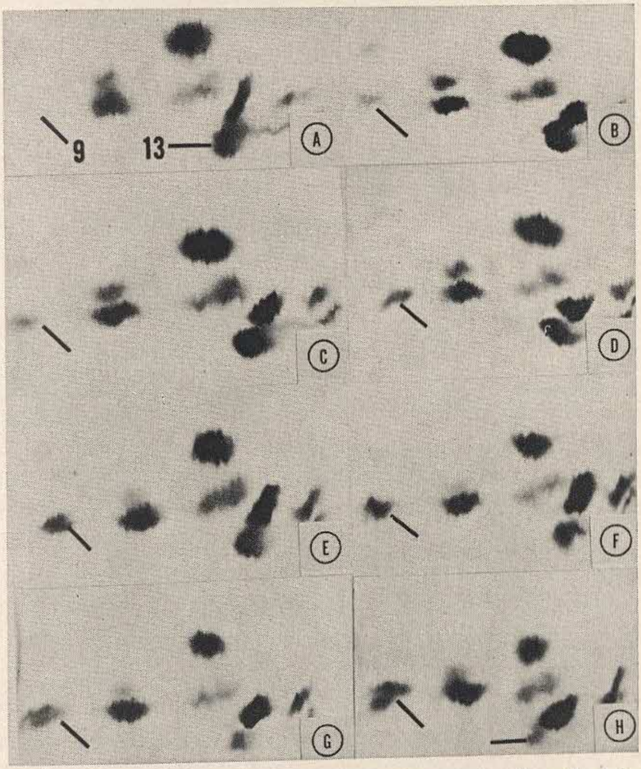

FIGURE 81. Amino acid patterns of extracts (20 mg.) of optic lobes of chick embryo brain at different days of incubation. (*A*) 6 days, (*B*) 8 days, (*C*) 10 days, (*D*) 13 days, (*E*) 17 days, (*F*) 19 days, (*G*) 20 days, and (*H*) 21 days. On patterns (*B*) to (*H*), the lines at position 9 point to GABA and the lines at position 13 point to ethanolaminephosphoric acid. Reprinted, by permission, from Sisken, B., Roberts, E., and Baxter, C. F.: Gamma-amino-butyric acid and glutamic decarboxylase activity in the brain of the chick. *Inhibition in the Nervous System and $\gamma$-Aminobutyric Acid*. E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 219).

which are in the process of preparation for detailed publication. To our knowledge, this is the first time that determinations have been made of enzymes which form and utilize a particular substance as well as of the substance itself in the course of the development of a specific structure of the central nervous system. The results show that the GAD and GABA-T activities and GABA levels increase progressively with development in the chick optic tectum in a similar manner. It is interesting that the largest increment in the mass of the optic tectum occurs in the period prior to the beginning of the time during which the greatest rate of

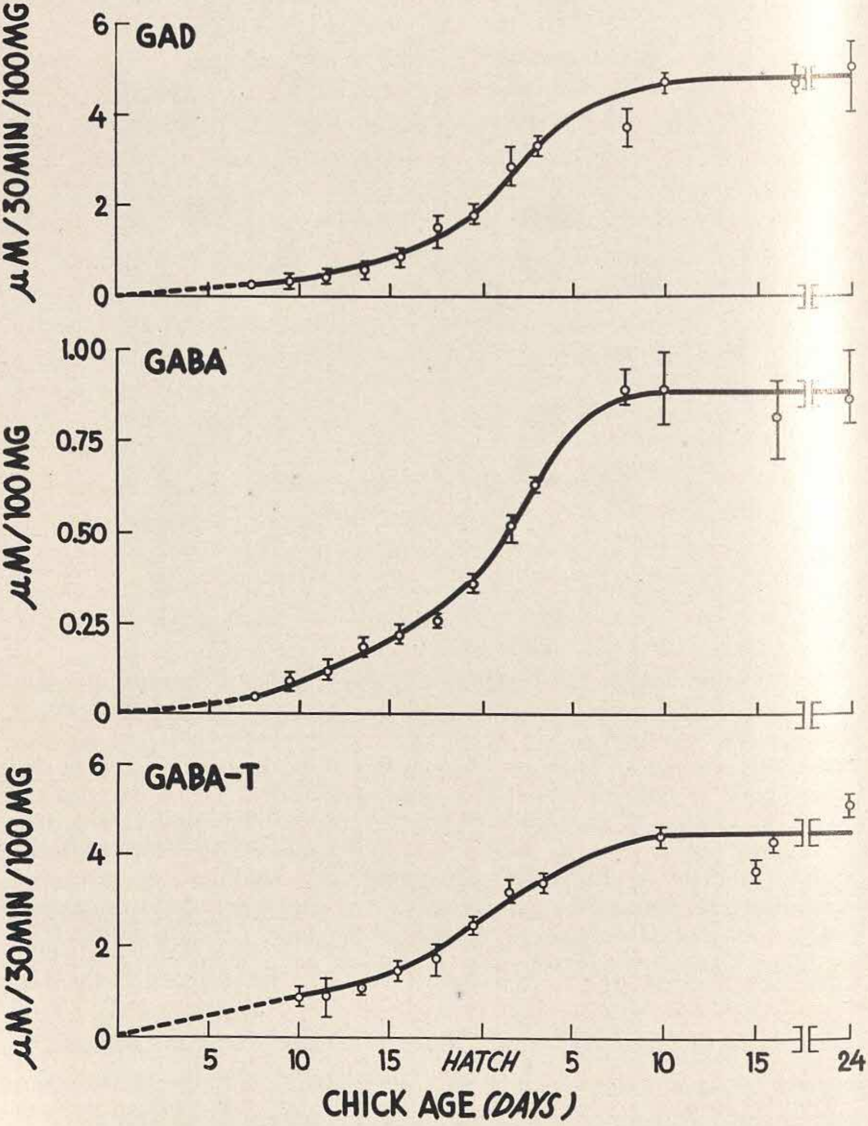

FIGURE 82. Changes with age in glutamic acid decarboxylase (GAD) and GABA-transaminase (GABA-T) activities and GABA content in the optic lobe of the chick. Where ranges are indicated, the averages were from four to five separate determinations. (Sisken, B., Sano, K., and Roberts, E: Unpublished data).

increase was noted in the biochemical variables studied, the structure attaining 60 per cent of its maximal weight at 15 days of incubation. The increases in the components of the GABA system take place at the same time that many other maturational changes are occurring in the optic tectum. Preliminary analysis has not revealed a particular variable which can be measured by histological methods or well correlated with the changes in the GABA system.

Although the shapes of the curves for the variables studied have a formal similarity to those obtained in adaptive enzyme formation in various systems, the present data neither support nor negate the possibility that the development of GAD and GABA-T are of an adaptive nature. It is not clear at the moment how experiments could be set up to test such a possibility. In contrast to the work with whole mouse brain, the *rate of increase* in the actual content of GABA in the optic tectum of the developing chick was virtually identical with that of GAD activity. Our results also indicate that it is not possible to generalize the results from one brain area to another with regard to these variables, since in other areas of chick brain studied, such as the hemispheres, cerebellum, diencephalon, and hindbrain, the rate of increase of maximal potential GAD activity after hatching was much greater than the rate of increase in GABA content (76).

The question might legitimately be asked why the content of GABA should increase if both the enzyme forming GABA and the enzyme utilizing it are increasing at a similar rate. It must be recalled that the measurements of both enzyme activities were made employing optimal conditions under which these enzymes were maximally active. The pH optima for the two enzymes differ widely (72). The substrate concentrations which are found in the cells are below those required for maximal activity of both enzymes, the level of GABA at all times being considerably below that of glutamic acid, the substrate for GAD. GABA-T requires the presence of relatively high concentrations of both GABA and $\alpha$-ketoglutarate for maximal activity. Early in development, when GABA levels are very low, it would be anticipated that the activity of the GABA-T in the living cell would be considerably below its maximal potential activity, especially since the concentrations of $\alpha$-ketoglutarate probably are considerably lower even than those of GABA. It is also possible that both GAD and GABA-T are located at different intracellular sites and that the availability of substrate for both of the enzymes might be limited by rates of diffusion from the sites of formation of the substrates. From the above discussion, it is apparent that at the present time there is insufficient knowledge of the pertinent intracellular variables to estimate to what extent the maximal potential activity measured in homogenates reflects the actual activity of the enzymes *in vivo*. However, the enzyme measurements are proportional to actual apoenzyme levels in the cell and to this extent probably furnish a valid measure of the rate of increase of the *potentially* active enzymatic proteins.

We may have, for the first time, an opportunity of determining whether the metabolic systems related to GABA can be correlated with some behavioral phenomena that are susceptible to quantitative treatment, such as imprinting.

The reason for thinking in these terms is that we can now lower or raise GABA levels in brain experimentally. They can be lowered by the administration of some hydrazides or antivitamin $B_6$ agents. They can be raised by the administration of hydroxylamine. It has been possible to achieve these alterations in GABA levels by affecting the enzyme systems we have just discussed, and it is feasible to attempt to do this at different times during development. I think that it would be possible to raise or lower GABA levels at the very periods which are critical for imprinting to take place. It would then be interesting to see whether the imprinting and GABA levels would have any relation to each other. Perhaps no relation would be found, and even that would be interesting. Since accurate measurements can be made both of the biochemical and behavioral variables, perhaps these points can be discussed later.

*Purpura:* Have you and your colleagues looked at the effects of hydroxylamine on reticulocortical activation? What I am concerned about is the possible "toxic" depressant effect of hydroxylamine which might limit its usefulness in the imprinting experiments.

*Roberts:* We found that the maximal effect in rats takes place in about 1½ hours. In chicks, we would have to find a dose which would be judged to be not particularly toxic and yet would have a measurable effect on GABA levels. Hydroxylamine causes methemoglobinemia. However, when extensive methemoglobinemia was produced by a variety of other agents in our laboratory, elevations in GABA levels or the associated changes in electrophysiological measurements were not observed. Hydroxylamine is the only agent which we have found to raise GABA levels significantly with little observable toxicity, although we have tested many other substances for this effect.

*Leake:* In connection with a method of increasing the rate of GABA formation, is it influenced by the administration of glutamic acid?

*Roberts:* Glutamic acid does not penetrate the blood-brain barrier quantitatively in mature animals as far as we know. We have not yet injected glutamic acid into chick embryos. The results presented here will serve as a control series for future experiments.

We have performed preliminary experiments in which we have injected hydroxylamine intravenously into chick embryos and have shown that some depression of GABA-T could be achieved, but we have not yet measured the effect on GABA levels.

I am grateful to Dr. Purpura for bringing up his reservations. We have been careful to indicate that we are dealing with correlations and not causal relations when biochemical effects are being observed after the administration of pharmacologically active substances.

*Reynolds:* May I ask what you meant by the statement that glutamic acid did not get in quantitatively?

*Roberts:* The glutamic acid level in the brain is not changed by the intravenous injection or feeding of glutamic acid to mature animals (74). However, there appears to be a relatively rapid exchange of radioactive glutamic acid across the blood-brain barrier (40). Although these results suggest that the total amount of glutamic acid which is available as substrate to GAD for the formation of GABA is not increased by injecting glutamic acid, the possibility exists that there are separate pools of glutamate. The glutamic acid which exchanges from the blood into brain tissue might actually be in a different pool from the glutamic acid which is ordinarily available as substrate for the action of GAD.

*Reynolds:* It has been reported, though, that the infant when fed glutamic acid builds it up to very high levels in the brain.

*Roberts:* There was no increase of glutamate concentration in the brains of rats or mice that could be detected by analytical procedures when considerable elevation of blood glutamic acid had been achieved. However, there was a considerable increase of glutamine content in brain when glutamine was administered intravenously (74). An important limitation on the formation of GABA might be the availability of glutamic acid as substrate for GAD. A number of experiments have suggested that under normal conditions GAD might be the rate-limiting reaction of the GABA shunt. If one assumes an average concentration of 0.01 M for glutamate in the central nervous system and a uniform distribution both for glutamate and GAD throughout the cell, one could calculate from the Michaelis constant of the enzyme ($6.4 \times 10^{-3}$ mol/liter) that the GAD would be operating at a somewhat greater than half-maximal rate, but not at full capacity. A decrease in the level of glutamic acid probably would decrease the rate of formation of GABA and the rate of operation of the full metabolic sequence. However, it is unlikely that both GAD and GABA are uniformly distributed throughout the cell substance in a neuron. It is possible that the enzyme is present in a milieu containing either more or less glutamic acid than is present in some other part of the cell. In all probability there exist unequilibrated pools of glutamic acid within nerve cells. How one would obtain information which would be related meaningfully to this sort of problem at the present is difficult to conceive.

*Keller:* What was the nature of the electrophysiological changes?

*Roberts:* We ourselves have not performed such measurements. A study has been published on this subject by Peters, *et al.* (53). However, the findings of the latter workers do not allow any correlations to be made with the measurements which we have performed on the GABA system. I have been told by neurophysiologists that gross electrical measurements made in developing chick embryo brain would be difficult to interpret in functional terms. I hope that we can bridge the gap between behavior and biochemistry by trying to relate some of our findings to behavioral observations, like imprinting, without necessarily interposing electrophysiological measurements for the time being.

*Hess:* Can you tell me how long the effect that you produce by changing the level of GABA will actually be?

*Roberts:* Inhibition of GABA-T was found to persist in some instances for as long as 24 hours after the injection of hydroxylamine in chick embryos. We hope that a similar result may be obtained with newly hatched chicks with the proper doses of hydroxylamine.

*Hess:* And how far can you either increase it or decrease it?

*Roberts:* This could only be a matter of conjecture. It would certainly depend on the age and relative activities of the enzyme systems as well as the areas of the brain which were being analyzed.

*Fremont-Smith:* Can you double it, for instance, or triple it?

*Roberts:* Yes, we have been able to double and even triple GABA levels in some experiments with mammalian systems, but I don't know about the chick. I think, however, that we can set up suitable experiments to find out whether we can raise the levels sufficiently to warrant carrying over the work into behavioral studies.

*Magoun:* How long a period of the chick's development is necessary to determine the imprinting procedure?

*Hess:* We have been finding that for imprinting, which is the learning of the mother figure, so to speak, the maximum effect is at the first day, or some time during the first day.

*Magoun:* For what fraction of the day do you need to maintain the situation to produce the result?

*Hess:* It would be good to have it for the complete 24 hours of the first day, but there is also a specific learning which is maximal on the second day. This relates to the home area of the animal, and, on the third day, there is maximal learning for food objects which is extremely significant. We have been working on this more intensively, lately, because it seems so peculiar that there is a maximum learning peak, for each of the three different activities of the animal, coming at three different times, and, fortunately for the chick, in the proper sequence. I think, if this can be done, it might be extremely interesting to work, not just with the kind of imprinting which you perhaps know, but with the other two kinds of apparent imprinting effects, except that psychologists feel they are much closer to association learning, especially in relation to food learning. It might be better to work with all three types of these behaviors, which are very clear-cut and easy to observe; also, it is possible to run many animals. We can do this in the food learning study, for example, train a hundred animals in a matter of a couple of hours, and test them and do all this within the period of a single day, which makes it very convenient. But we will have a chance to talk about this later.

*Hinde:* Dr. Roberts, I'm not quite clear why, in the hope of getting a correlation, you choose imprinting, for which there is a sensitive period. You could use some more easily measurable type of behavior that goes on the whole time, like the "lost cheeping" call which birds give when isolated. What is your rationale for choosing imprinting?

*Hess:* This would be measured automatically. Of course, all this information would be obtained in experiments on imprinting. This information is a by-product which might be a great deal more useful later on than what you had intended to measure in the first place.

*Hinde:* So there is no particular significance in choosing something which appears to have a sensitive period?

*Roberts:* I think there is, because there is still a rapid rate of change of these things at that particular period.

*Hess:* Of course. That is the whole idea.

*Roberts:* The curves for GAD activity and GABA levels as a function of time are just below the inflection points at the time of hatching (Figure 82), so that these variables are undergoing their most rapid rate of change approximately at the time that imprinting takes place. A change in GABA levels up or down at this sensitive period, when a new behavior is appearing which is measurable, should give us a good opportunity to test whether a correlation exists.

*Hinde:* I would have thought that there were other types of behavior which are present throughout this period and whose variation you could measure equally profitably.

*Roberts:* I know so little about valid quantitative measures of behavior in general, that I suppose I really thought about imprinting because I knew about it, but not about other types with which I am not familiar.

*Hess:* As I understand what has been said, a reason for working with imprinting (or, let's say, behavior during the first few days, regardless of the imprinting aspect) is that there seems to be a chemical phenomenon which is at its peak in the first day or so and which then levels off approximately at 4 or 5 days and stays there for 2 weeks afterward.

*Roberts:* No, the GABA levels and the activities of the two enzymes chiefly involved in its metabolism are close to the adult level at 5 to 6 days after hatching.

*Hess:* I see. It continues and stays at that same level? So that if one were to make a guess as to what is a good behavior to correlate with this change, I would probably say the best guess is the development of fear in the chick. This reaches a maximum at about the same time that GABA reaches a maximum. I just want to reassure Dr. Roberts that I'm not "hipped" on imprinting.

*Doty:* There is one other difficulty which Dr. Roberts has referred to, however; the compound, hydroxylamine, does other things besides inhibiting GABA. It inhibits, for example, the increased oxygen uptake of nerve pursuant to activity (15).

*Roberts:* It does?

*Doty:* Yes.

*Roberts:* I would guess that the effect would depend on the quantity of hydroxylamine employed. We have produced effects with relatively small amounts. Our goal is to get the maximal effect with the minimal dose of drug, and, of course, we must be aware constantly of the reservations about the procedures employed. In addition to increasing the pyridoxal phosphate requirements, vitamin $B_6$ antagonists and hydrazides could produce myriad other effects. As soon as a compound which is alien to a particular area of the nervous system is introduced, there is the possibility of many effects. As long as this is kept in mind, we will not be in any great danger of making bad mistakes. The experimental results are reproducible, although the interpretations may change with time.

*Windle:* Dr. Roberts, is there any way you can relate the rather rapid rise in the curve to behavioral phenomena in any mammal?

*Roberts:* I wasn't personally aware of behavioral variables which could be employed extensively for experimental measurements during this period of development in mammals, but I am sure they probably exist. However, I am not familiar with the literature in this general area, and I was much impressed by the accurate and extensive studies done with fowl (27).

*Windle:* Of course, the unfortunate thing about the fowl is that you can't go earlier than hatching.

*Roberts:* You can.

*Windle:* You can? Do you have surviving chicks prior to hatching?

*Hess:* How long before it ordinarily hatches would you take out the chick? It wouldn't survive unless you took it quite close to hatching time. But what chance is there of a mouse surviving?

*Windle:* There is a considerable chance. Let's not talk about the mouse, but there is considerable chance that a monkey will survive. A monkey is born after 168 days gestation, and we have had a survivor at the 144th day. I would suggest, though, that a more primitive mammal might be appropriate, and that the opossum is ideal, for it is born after only about 13 days in the uterus; in the pouch it can be experimented on for weeks. This, incidentally, is a species that has too long been overlooked for experiment.

*Purpura:* While we are on this subject we should not overlook Langworthy's contribution, especially his early work with the immature opossum (41).

*Roberts:* The curves of the GAD and GABA-T activities which have been shown previously as a function of the time-course of development in the optic tectum of the chick embryo must be interpreted with reservation. We do not know that the maximal potential activities which we had measured are proportional to the activities of these enzymes within the cell. It has not yet been determined whether there is enough pyridoxal phosphate to saturate both enzymes in the living state, or whether there is sufficient substrate to keep the enzymes operative at maximal capacity. The interpretations must necessarily be limited by the techniques which we have had to employ. However, it is now feasible to begin *in vivo* work with avian material. Intracerebrally injected $C^{14}$-labeled glutamic acid or GABA, both of which have been shown in the case of the mouse to be utilized rapidly *in vivo* (72), also can be employed in the chick embryo to obtain some idea of the relative rates of transformation of these substances at various stages of development.

The measurements made of GABA, a simple molecule determined by a specific analytical method, represent the actual amount of the substance present at the various developmental stages studied. It is not known, however, whether GABA is distributed uniformly throughout the cell, whether it is concentrated near neuronal membranes and in the dendrites, etc., or whether it is present in one type of neuron and not in another. The answers to these questions will have to await improvements in our techniques of localization of simple substances within neurons.

The amount of GABA present at any time in a particular area of the central nervous system is probably a reflection of the balance between the rate of formation and the rate of utilization. Parenterally administered GABA does not appear to enter the brain readily (71).

Intravenous injection of as much as 3 gm./kg. of GABA into mice produced no change in the GABA levels of whole brain. Similar results were obtained when GABA was injected intraperitoneally into rats. At a time when the blood level was high, no GABA was detectable in the cerebrospinal fluid of an unanesthetized monkey which had been given 200 mg./kg. of GABA (84). These findings suggest that GABA does not readily pass the blood-brain barrier. However, physiologically disturbed or diseased areas of brain might allow passage into cerebral tissue of blood-borne GABA. Electrophysiological evidence indicates that systemically administered GABA ordinarily does not pass the blood-brain barrier in the cat, but that following experimental local breakdown of the barrier, penetration of intravenously injected GABA does take place (65).

The GABA system is definitely intracellular, and studies which have been done on the localization of the system suggest that it is probably neuronal and not present in glia, astrocytes, or myelin (1,44). The formation of GABA from glutamic acid can be inhibited preferentially by some convulsant hydrazides like thiosemicarbazide and vitamin $B_6$ antagonists. Such an interference has been generally correlated with increased sensitivities of various areas of the central nervous system to stimulation and with the occurrence of seizures. Administration of thiosemicarbazide was found to decrease the rate of conversion of intracerebrally administered L-glutamic acid-U-$C^{14}$ to GABA (Table I) and to lower GABA lavels in various areas of brain (Table II).

Five mice received 0.4 mg. of thiosemicarbazide intraperitoneally 15 minutes prior to intracerebral administration of 0.03 ml. of $C^{14}$-labeled glutamic acid. The animals were killed and the brains removed for analysis 30 minutes after glutamic acid was given. No convulsions occurred during the study. A group of control mice received only glutamic acid 30 minutes prior to removal of brains. The results show

## TABLE I

**Glutamic Acid/GABA Ratios in Extracts of Mouse Brains 30 Minutes after Intracerebral Injection of L-glutamic Acid-U-$C^{14}$**

| Treatment | Glutamic acid/GABA | |
|---|---|---|
| | Molar | Radioactivity |
| Controls | 3.9 | 4.7 |
| | 4.6 | 4.0 |
| | 3.0 | 3.4 |
| | | 4.2 |
| | 2.5 | 4.0 |
| Average | 3.5 | 4.1 |
| Thiosemicarbazide | 4.0 | 7.1 |
| | 3.4 | 15.9 |
| | 3.5 | 7.6 |
| | 4.2 | 11.2 |
| | 3.7 | 13.1 |
| Average | 3.8 | 11.0 |

Reprinted, by permission, from Roberts, E., Rothstein, M., and Baxter, C. F.: Some metabolic studies of γ-aminobutyric acid. *Proc. Soc. Exper. Biol. & Med.* 97, *796-802 (1958).*

that the amount of glutamic acid relative to GABA was not increased significantly by thiosemicarbazide. However, a highly significant increase in ratios of radioactivities of these two amino acids was noted, showing decreased rate of flow of isotope from glutamic acid into GABA (72).

GABA-T, the system which is believed to be chiefly responsible for the metabolic utilization of GABA, can be blocked preferentially by

## TABLE II

**Influence of Hydroxylamine ($NH_2OH$) and Thiosemicarbazide (TSC), Alone and in Combination, on GABA Levels in Rat Brain**

| Brain Area | GABA Levels (mg/100 gm of tissue, wet weight) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Control (5 animals) | | $NH_2OH$ only (3 animals) | | TSC only (4 animals) | | TSC ½ hr after $NH_2OH$ (4 animals) | | TSC + $NH_2OH$ together (5 animals) | | TSC ½ hr before $NH_2OH$ (5 animals) | |
| | Average for Group | Range | Average for Group | Range | Average for Group | Range | Average for Group | Range | Average for Group | Range | Average for Group | Range |
| Cortex | 25 | (24-27) | 49 | (45-54) | 18 | (16-20) | 43 | (45-57) | 41 | (36-45) | 37 | (28-47) |
| Medulla | 25 | (23-26) | 33 | (28-38) | 17 | (16-18) | 34 | (28-44) | | | 26 | (22-29) |
| Pons | 27 | (25-28) | 42 | (38-46) | 18 | (17-19) | 42 | (34-53) | 29 | (27-32) | 31 | (27-37) |
| Cerebellum | 27 | (25-30) | 37 | (35-38) | 20 | (19-23) | 44 | (38-51) | 37 | (30-49) | 38 | (29-43) |
| Hippocampus | 31 | (28-35) | 41 | (38-44) | 20 | (18-22) | 42 | (39-44) | 39 | (36-43) | 39 | (27-50) |
| Caudate nucleus | 31 | (29-33) | 46 | (42-52) | 22 | (20-24) | 45 | (31-54) | 41 | (33-55) | 43 | (29-51) |
| Olfactory lobes | 48 | (38-55) | 61 | (44-78) | 43 | (37-51) | 65 | (57-78) | 62 | (52-75) | 61 | (50-77) |
| Diencephalon | 53 | (46-60) | 71 | (62-75) | 32 | (27-36) | 66 | (54-88) | 57 | (52-63) | 56 | (42-71) |
| Colliculi | 56 | (52-60) | 85 | (77-95) | 33 | (31-35) | 73 | (60-94) | 58 | (54-65) | 53 | (38-66) |

All animals receiving TSC went into convulsion. Animals receiving $NH_2OH$ only, were sacrificed at 90 to 120 minutes after injection. All animals receiving TSC, alone or in combination with $NH_2OH$, were sacrificed at time of first maximal tonic convulsion.

hydroxylamine. This results in the increase in levels of GABA in various areas of brain in rats [(3), Table II], cats (17), and monkeys (Table III) and in decreased sensitivity to stimulation in various areas (Figure 83) (67).

Although such correlations have been demonstrated convincingly, experiments have been completed recently in our laboratory which demonstrate that the physiological effects of thiosemicarbazide, one of the most effective convulsant hydrazides, cannot be attributed solely to its effect upon the systems involved in the metabolism of GABA (4). Thiosemicarbazide, when administered alone, lowered the levels of GABA in nine areas of rat brain which were studied, while hydroxylamine alone elevated them in all cases (Table II). However, when animals received both thiosemicarbazide and hydroxylamine,

TABLE III

**Effects of Hydroxylamine ($NH_2OH$) on GABA Levels in Three Cortical Areas of the Macaque Monkey**

| Cortical Area* | Dose of $NH_2OH$ (mg/kg) | GABA Levels Found (mg per cent) | |
|---|---|---|---|
| | | Before $NH_2OH$ | 90 min after $NH_2OH$ |
| Monkey 1 | | | |
| Motor | 4.8 | 15.5 | 22.6 |
| Parietal | 4.8 | 12.4 | 21.7 |
| Occipital | 4.8 | 14.1 | 25.5 |
| Monkey 2 | | | |
| Motor | 7.2 | 14.9 | 34.1 |
| Parietal | 7.2 | 14.7 | 35.5 |
| Occipital | 7.2 | 13.6 | 40.2 |

*One sample of each area was removed before intravenous administration of $NH_2OH$ and the other was obtained from the opposite side (homotopic) 90 min after $NH_2OH$ was injected.

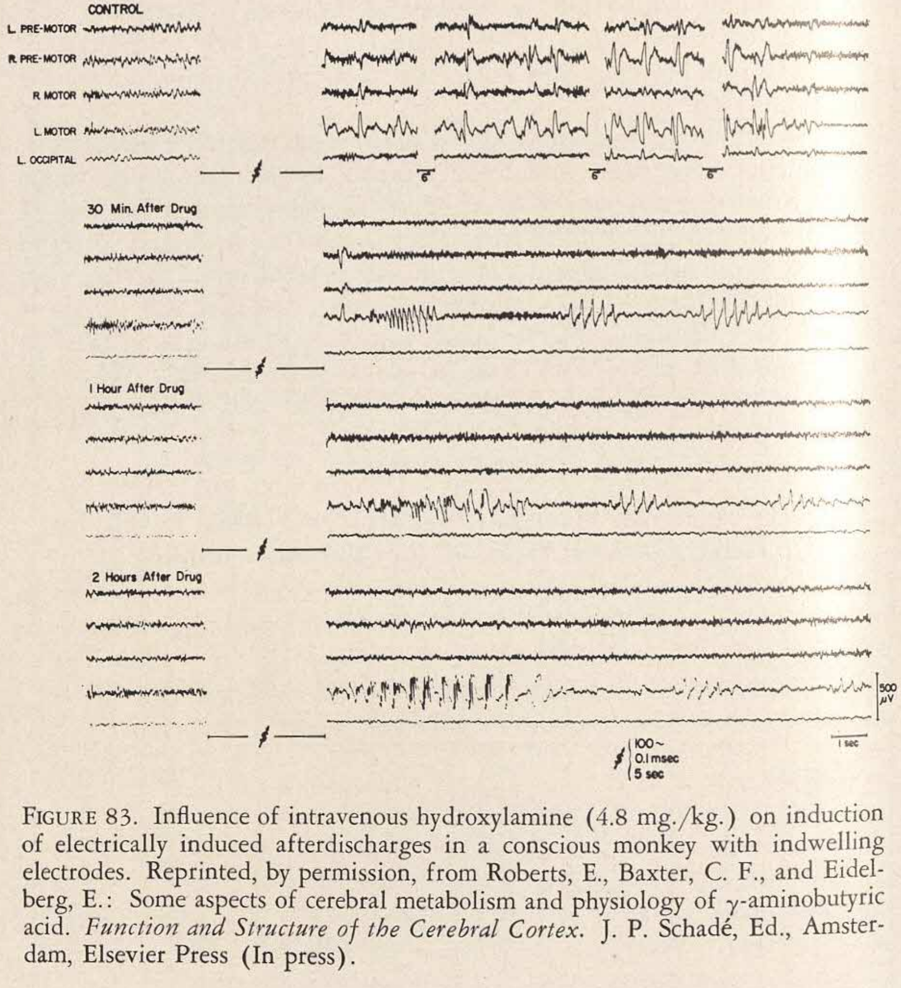

FIGURE 83. Influence of intravenous hydroxylamine (4.8 mg./kg.) on induction of electrically induced afterdischarges in a conscious monkey with indwelling electrodes. Reprinted, by permission, from Roberts, E., Baxter, C. F., and Eidelberg, E.: Some aspects of cerebral metabolism and physiology of $\gamma$-aminobutyric acid. *Function and Structure of the Cerebral Cortex.* J. P. Schadé, Ed., Amsterdam, Elsevier Press (In press).

seizures occurred which in time of occurrence and intensity were characteristic of those usually produced by thiosemicarbazide alone, but in all instances the areas of brain studied showed either normal or elevated levels of GABA. These results indicate clearly that an over-all depression of GABA levels is not a necessary requirement for thiosemicarbazide-induced convulsions, a conclusion in keeping with the recent physiological experiments (16,83). According to the simplified scheme shown in Figure 84, it may be postulated that in addition to inhibiting the GAD system (action one), thiosemicarbazide may have some other direct or indirect excitatory effect on neuronal

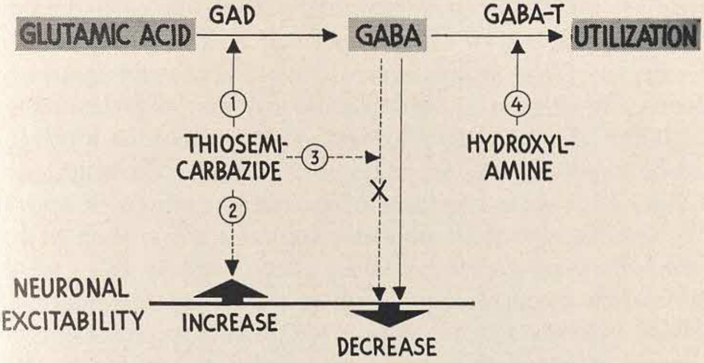

FIGURE 84. Simplified scheme showing a rationalization of the effects of thiosemicarbazide and hydroxylamine on neuronal excitability and the GABA system.

membranes (action two), or may inhibit one or more systems which are involved in the formation of some substance, X, from GABA (action three); this might have more potent inhibitory effects in the central nervous system than GABA itself. In this connection, the recent isolation of γ-aminobutyrylhistidine from brain is of interest (56). The physiological properties of the latter substance have not yet been studied. According to the scheme, an increase in GABA resulting from an inhibition of GABA-T (action four) by hydroxylamine would cause a decrease in neuronal excitability either because of the action of increased concentration of GABA directly or because of the possible enhancement by increased substrate level of the formation of an active derivative of GABA. In the experiments when both thiosemicarbazide and hydroxylamine were injected, the elevations of GABA content noted in most areas of brain indicate that the *relative* decrease in GABA-T activity produced by hydroxylamine was greater than that produced in GAD activity by thiosemicarbazide. The occurrence of seizures in these animals could result from effects of thiosemicarbazide which are not necessarily related to inhibition of GAD, as indicated in Figure 84.

It should be emphasized that the above results do not preclude the potential usefulness of elevating the endogenous GABA levels in the central nervous system as a tool in studying effects on behavior as well as a means of treatment in some clinical disorders in man. At the present time, the results obtained with the mammalian nervous system are incompatible with a transmitter function for GABA, but are in keeping with the role of a modulator of neuronal excitability which is produced and which exerts its effects intracellularly (12). The view has been expressed that GABA is more likely a membrane "stabilizer" rather than an inhibitory transmitter. Administration of hydroxylamine has produced elevations of GABA levels as well as powerful anticonvulsant effects. Gross behavioral changes, especially passivity and disappearance of aggressive behavior, were observed in Macaque monkeys which had been given small doses of hydroxylamine intravenously. It would be expected that elevations of GABA levels might decrease susceptibility to a wide spectrum of excitatory influences and should enhance the effectiveness of pharmacological agents, such as barbiturates, which may counteract excitatory effects. Along this line, it now has been shown in experiments with rats that pretreatment with hydroxylamine in doses (19 to 49 mg./kg.) which produce increases in GABA levels in brain resulted in a remarkable decrease in the animals' susceptibility to seizures induced by the administration of metrazol (67).

The strategic problem that arises in the case of interpreting the action of hydroxylamine is similar to that previously discussed for thiosemicarbazide. Although a correlation has been found in the occurrence of decreased neuronal excitability and elevation in content of GABA when hydroxylamine is administered, a causal relation cannot be inferred. Hydroxylamine may have many effects on the central nervous system in addition to the inhibition of GABA-T. Whether or not the anticonvulsant and behavioral effects can be attributed solely to the elevation of GABA in the central nervous system cannot be determined from the measurements which have been made to date. It would be helpful if several chemically different inhibitors of GABA-T were available on which similar studies could be performed.

*Leake:* Confining our thought now to GABA within the cell and the ways by which it may be raised or lowered in amount, hydrazides lower GABA content, and, if it is assumed, then, that the GABA content is correlated with a general inhibitory activity on the function of the cells of the brain cortex, this action of the hydrazides correlates with their over-all pharmacological behavior pattern, in so far as they become what are called now psychic energizers. Does that follow?

*Roberts:* Some of the hydrazides which are "psychic energizers" are di-substituted hydrazides and these di-substituted hydrazides act differently from the mono-substituted hydrazides, which react with the aldehyde group of pyridoxal phosphate. The field has become even more complicated. Hydrazides can react with the aldehyde group of pyridoxal phosphate to form derivatives which are inactive as coenzymes, thus decreasing the activity of the GAD and other $B_6$-requiring enzymes. Some of the products formed by the interactions have been found to be extremely potent inhibitors of pyridoxal kinase, the enzyme which catalyzes the synthesis of pyridoxal phosphate from pyridoxal and adenosine triphosphate (47). So now we may consider that the hydrazides and related substances not only decrease the GAD activity (and possibly the activity of other pyridoxal phosphate requiring enzymes), but that they may actually stop the formation of the coenzyme from the available dietary forms of vitamin $B_6$, thus putting an additional blockade on the reconstitution of the active holoenzyme.

*Fremont-Smith:* Do they also block the formation of the derivative?

*Roberts:* No, the derivative is the inactive form. This is just a chemical reaction. The kinetics of the physiological effects shown by the convulsant hydrazides must, therefore, be extremely complex. In view of some of the foregoing discussion, it now appears naive to think that biochemical effects such as the inhibition of GAD *in vivo* and decreases in GABA levels resulting from the administration of the convulsant hydrazides are causally related to the physiological effects which are observed, such as gross convulsions or paroxysmal discharges on EEG recordings. We are working hard at this moment to find more ways of breaking the correlation rather than reinforcing it so that we may obtain further insights into the operation of the system.

*Leake:* And yet, the correlation in general stands that increased GABA levels go along with increased evidence of inhibitory activity?

*Roberts:* Yes, that's right.

*Leake:* And lowered GABA levels go along with decreased evidence of inhibitory activity. The point I was trying to make is simply that there is nothing that has been found so far to interfere with your general over-all concept that GABA is essentially an inhibitory factor in the central nervous system.

*Roberts:* Yes. However, by saying that GABA is an inhibitory factor we must realize that we know little or nothing about the mechanism at a molecular level. We do not know whether GABA itself is doing the acting or whether something has been formed from GABA in the area in which the GABA is effective. Perhaps one of the things that is of most concern to us at this time is to prevent the development of a cant about the GABA field which would make it difficult for progress to occur. We want to keep all the lines free and just discuss the observations which actually have been made, their validity, and their possible meaning.

*Purpura:* Dr. Roberts, it should be pointed out that there are very few areas of general agreement concerning the role of GABA in the functioning of the nervous system. Dr. Roberts and his staff at the City of Hope, together with Dr. Killam, Dr. Adey, and Dr. van Harreveld, organized a splendid conference on the subject of *Inhibition in the Nervous System and γ-Aminobutyric Acid* in 1959, and the record of this conference is now published. To mention even a few of the areas of disagreement would take up much time, for there is certainly disagreement concerning the relationship between "brain excitability" and GABA-concentrations, and the interpretation of GABA-effects on spinal neurons and cortical evoked potentials. While we are far from knowing all the facts on the role of GABA in the functioning of the nervous system, a good start has been made in this direction, as you have indicated.

*Windle:* Is there any information on whether or not GABA has anything to do with the activities of the neuroglia?

*Roberts:* We are hoping to get some pure tissue cultures of glia to see if we can detect the GABA system in them by micromethods now available for measurement. Published work seems to indicate that the GABA system is probably neuronal (1,44).

It is almost certainly intracellular. There is no evidence that GABA, which is formed in the brain, can leave the brain readily and enter the blood. It has not been found in spinal fluid, even in patients with massive head injuries. It certainly would not appear to be floating on the surface of the brain.

With regard to what Dr. Purpura said, I tried to indicate to you how difficult this problem is. We must keep on making valid measurements and maintaining an open mind as far as interpretation of the results is concerned. What is hopeful to me is that physiologists and chemists and even physicians are talking and thinking about the same things.

*Leake:* Do these endogenous changes with GABA that you have been working with reflect at all on the polarity changes on the membrane?

*Roberts:* So far as I know those who have worked with the individual neurons employing the crustacean structure have not tested hydroxylamine on the system.

*Purpura:* Dr. Leake has touched on one of the major problems which confronts all of us who are interested in attempting to define the relationship between changes in endogenous GABA and pharmacological effects of the amino acid on the surfaces of neurons. There is little doubt that GABA is intracellular and Dr. Roberts feels GABA is largely free or unbound. What pharmacological effect could GABA have inside the neuron? It is known that injection of a variety of potent toxic compounds and pharmacological agents inside axons produces very little change in resting potential and excitability. In the studies of

Brady, Spyropoulos, and Tasaki (8), no effects were observed on resting and action potentials of single squid axons following intracellular injection of cyanides, as well as LSD and other potent pharmacological agents.

Curtis and Watkins reported (12) that iontophoretic injection of GABA into motoneurons produced little change in the excitability of these elements whereas when GABA was applied to the surface of motoneurons the latter exhibited depressed excitability to orthodromic and antidromic stimulation. These effects of GABA on motoneurons are quite different from those which we have observed on cortical neurons (62,64). However, motoneurons in the spinal cord may have fundamentally different properties from cortical pyramidal neurons. This may be one of the reasons for the differences between the results of Curtis and Watkins and our own findings.

*Roberts:* At the moment, this is not something that can be approached experimentally.

*Purpura:* The problem of where and how GABA is acting is an important one. There is little doubt that the effects of pharmacological agents on nerve cells are exerted exclusively on surface receptors. What can one deduce about increases or decreases in total GABA concentrations of brain samples? Very little, I think, but this only emphasizes our current confusion. When GABA is increased after hydroxylamine, probably other constituents of brain are altered also. The net effect of injecting hydroxylamine appears to be a decrease in cortical excitability and it seems to me that it cannot be assumed that the change in cortical excitability is solely attributable to an increase in GABA content.

*Bodian:* I wish you wouldn't put so much emphasis on the negative effects of injecting substances within the neuron. Some cells are capable of ejecting materials that are injected this way.

*Purpura:* This is an important point. It has been claimed that curare fails to block axonal conduction because the drug cannot penetrate the lipid barriers surrounding the axon and get to acetylcholine receptors on the excitable membrane. What I am pointing out is that Brady, *et al.* (8) and other workers have shown that drugs which have little action when applied to the external surface of cells are also ineffective when injected intracellularly. It is possible that intracellularly injected compounds fail to gain access to the excitable membrane because of a barrier inside—

*Bodian:* I realize that, but I think the positive effects are more important. With the negative effects of injection, there seems no way to be sure that artifact has not entered the picture. Also, there is nothing to measure.

*Sokolov:* I would like to make some remarks about excitation and the measurement of excitability. All the results to be obtained with GABA have been related to aspects of measurement of excitation in the cortex. It is very interesting that external stimulation (by light or sound) sometimes results in a decrease of the response. This decrease of the dendritic potential has been interpreted as a decrease of excitability.

In studying stimulation of the cortex by flickering light, we have observed that under the influence of certain external stimulation, there is a drop in amplitude of the driving response. However, at the same time, there is a shortening of the excitability cycle. For example, in the absence of arousal by external stimulation, the response may have a period of perhaps 100 msec., but after arousal, the period of response to the same flicker is shorter, and the amplitude is smaller, too. Therefore, in my view, amplitude alone is not an adequate sign of excitability level.

You have shown us that under the influence of GABA, there is a decrease of the response to stimulation. The frequency of the stimulation is very important. For example, we have very often observed that the amplitude of the cortical response to slow rates of flicker is decreased, whereas when we stimulate with high frequencies of light, the same arousal response produces an increase in amplitude (13,78,79).

My idea is that the dendritic response, according to the previous discussion at this conference, is influenced by some kind of inhibitory neural cell in the cortex analogous to the Renshaw cells for the regulation of the motor neuron. This idea was expressed at a previous Macy conference by Dr. Purpura (61). I believe that this decrease in amplitude with the accompanying decrease of the period of the response is connected with the intensification of the negative feedback through the activation of this kind of inhibitory neuron, regulating the dendritic potential. In this case, the results of the administration of GABA can be looked at from a different point of view. GABA can stimulate not only excitatory cells but the inhibitory cell of the negative feedback as well, and the result of this activation is a decrease in amplitude and a more rapid response in the cortex.

Looked at from the point of view of transmission of information, we came to the conclusion that decrease of the period means that more "bits" of information can be transmitted. This statement uses the language of Information Theory which we find very useful for the understanding of the biological role of these phenomena.

I should mention the results obtained in Lindsley's (43) laboratory, which have shown that under the arousal response, two single flashes of light produce two single dendritic responses, whereas, without arousal, these two responses are integrated into one, with no discrimination being made between them. I believe that our results with harmonic analysis of the EEG are very closely connected to Lindsley's finding of this increase of discrimination power.

*Fremont-Smith:* You are saying that the frequency is much more important than amplitude, in terms of activity?

*Sokolov:* The frequency determines the amplitude. In an automatic regulator with negative feedback, increase of the frequency is connected with decrease of amplitude, but discrimination of the responses is higher. Therefore, the power to transmit information is greater and this is a most important function in neuronal activity.

*Roberts:* That is very interesting because, on the basis of an extensive distribution study, Dr. Elisabeth Florey believes that material which is extractable from mammalian nervous tissue and is inhibitory on the crayfish stretch receptor (Factor I) is present in particular, neurochemically differentiated neurons in the central nervous system (21). GABA (and other inhibitory substances) and specific neurons dealing with the inhibitory phenomena might be related or might have exactly that type of integrative function that you describe. I won't attempt to discuss this any further, since the subject is far beyond my own area of competence; however, I certainly appreciate this point of view. It is very interesting.

*Sokolov:* I believe it is this point of view that is the clue to understanding the increase of GABA content with maturation.

*Leake:* In any discussion of the biochemical maturation of the central nervous system, there should be some reference to the fine work of Heinrich Klüver, of the University of Chicago, on porphyrins in relation to the development of the nervous system (33-36). In studying fluorescent compounds acting on the central nervous system, he found that brain sections give characteristic fluorescent spectra. The white matter gives an emission band at 625 m$\mu$. There is no such emission in the gray matter. Extraction confirmed chemically the occurrence of coproporphyrin, and probably other porphyrins were also present in small amounts. Porphyrins have not been isolated from the peripheral nervous system. Klüver studied over 700 animal specimens and found porphyrin in various regions of the brain and spinal cord in forty-five species of mammals and birds. On the other hand, no porphyrins were found in the nervous system in fifteen species of reptiles, amphibians, and fishes. The mammalian and avian nervous systems do not contain porphyrins at birth. By fluorescent spectroscopy, it was found that the characteristic porphyrin emission band appears first in the spinal cord of 20-day old rats, and then appears successively in the fiber masses of the brain stem, the cerebellum, and the cerebrum. In the postnatal development of the central nervous system, therefore, there is an "ascending porphyrinization." This is observed in birds, as well as in mammals. Klüver raises the question of a possible relation between porphyrins and the processes of myelination. He thinks also that they may be related to the presence of oligodendroglia. These cells, as well as Schwann cells, pulsate as shown by C. M. Pomerat (58).

Klüver finds that the porphyrins in the central nervous system are remarkably stable, since no disease or lethal poison causes their disappearance or markedly affects their distribution. Fox (23) suggests the possibility that brain porphyrins are involved in the photostimulation of mammalian and avian sexual cycles. There are other fluorescent substances in the central nervous system, such as lipofuscin. Klüver indicates his indebtedness to the late Dr. C. Judson Herrick in connection with the distribution of various types of cells in the central nervous system. For example, oligodendroglia are absent from the nervous system of cold-blooded animals.

It is also interesting to report that in personal communications from Dr. Edward Kropa of the Battelle Memorial Institute, I have learned that porphyrin chelating compounds with various metallic ions possess semiconductor properties. Klüver's work on the porphyrins has been carefully controlled and reported in detail. He notes the occurrence of possible chelated zinc-porphyrin complexes in the brains of warm-blooded animals.

*Livingston:* Perhaps, some of the things that take place in the GABA evolution may also be related to the requirements imposed upon the animal by a change in his life situation, including the exposure to many stimuli and opportunities which become very much enlarged on the escape from the shell and so forth. Would you care to comment, Dr. Windle?

*Windle:* The phenomenon of arousal is a very interesting one. Of course, we have been aware of it for a long time. The mammalian fetus *in utero* is apneic and dormant; however, it can be aroused toward the latter part of gestation. If a needle is run through the belly wall and the fetus is touched, it will arouse. It does not normally execute respiratory movements *in utero*, but as birth becomes imminent, the dormant fetus will arouse during the birth process as the oxygen saturation of the blood reaching it declines.

This arousal takes place in the monkey. When fetal blood oxygen saturation declines to about 40 to 50 per cent, at which time the monkey will make respiratory movements, a second type of arousal is instituted; this is hypoxic or asphyxial arousal. Incidentally, there is a great deal of confusion in the clinical literature over this matter of arousal, and of apnea, with misinterpretation of physiological apnea as indicating anoxia.

If the fetus of a sheep is delivered into a warm bath and the oxygen supply maintained it is possible to keep the fetal lamb in a state of physiological apnea. If he is lifted out of the bath while records are being made electrically from the muscles, an active electromyogram results; and if he is put back into the bath, he will quiet down. However, when lifted out again, arousal results.

In the normal course of events, when a monkey fetus is delivered, the oxygen saturation of blood going to his brain drops from something like 79 per cent to a lower figure, say, 40 per cent, and then his respiratory mechanism is triggered and he starts to breathe. If his airways are open, of course, the saturation never gets below that level, and he is never anoxic. But if the airway is deliberately occluded, asphyxia sets in, and this respiratory pattern dies out. The monkey then becomes apneic again—asphyxial apnea—and resuscitation becomes necessary, for he will not begin to breathe.

*Brazier:* I think there is one other interesting piece of information which bears on the use of this word, "dormant" for the fetus. As I understand Lindsley's classic work (42) on the EEG of the human fetus *in utero*, he did not find sleep waves. He recorded waves which, to the electroencephalographer, contradict the concept of a dormant state.

*Leake:* This correlates, then, with the general developing idea of sleep as an active process, which matures much later than any other aspect.

*Windle:* In normal monkeys, EEG's taken on the first day were characterized by generalized flat, almost isoelectric activity. Tracings in the first week showed low voltages in all leads with some countable 4- to 6-per-second waves. During the second week, more marked changes appeared, especially during sleep, when higher voltages were observed in the frontal and parietal leads, with some bursts suggesting spindle formation. Around the third week, sleep patterns became more striking: high-voltage slow waves and paroxysmal discharges, irregular high-voltage waves of mixed frequencies, and some very sharp waves suggesting seizure discharges. Besides this paroxysmal activity, localized negative spike seizure discharges were also observed, these being most marked in the frontal and parietal tracings. Well-developed spindles (12 to 14 per second) were encountered in most monkeys near the end of the first month. The electrical activity in the normal monkeys not only varied with the state of wakefulness or sleep, but also showed maturational changes with age. EEG activity, comparable to that of the adult human subject, was observed at 40 to 60 days of age.

*Brazier:* It is certainly possible to obtain typical sleep EEG's from 1- or 2-day-old children, with complete "K complex" responses. But, as I understand it, Lindsley (42) did not find the sleep type of EEG in the recordings that he made from the human fetus.

*Reynolds:* I thought the point that Dr. Livingston was going to make was that this was a period of very rapid chemical changes in many constituents. Certainly, in the mammal, this is true. This loss of carbohydrate resources, in the guinea pig, at least, occurs in about 8 hours, from a very high level down to a virtually unmeasurable level. Blood sugar follows the same course. I think Needham's book (51) on chemical embryology has a lot of comparable data on the chick, does it not?

*Roberts:* Needham was quite unselective in his choice of data for that book. Although a great deal of literature was quoted, there were few attempts made at selecting and evaluating data on the basis of the methodology employed. For example, it would be necessary to consult the original references to find out whether valid methods were employed for the measurement of the sugar levels.

*Windle:* There are some chemical differences in the response of the fetus and the newborn to asphyxia. For one thing, the blood glucose of the fetus, suffering from anoxia, rises. In the newborn, made anoxic by immersion in nitrogen gas, it falls. The cardiac glycogen reserve of the newborn reaches a negligible quantity in a matter of seconds, whereas, in the fetus, the cardiac glycogen reserve is still measurable 2 minutes after anoxia, so there are chemical differences between the fetus and the newborn, regardless of what particular day birth is induced.

*Bodian:* I hope Dr. Livingston's point won't be overlooked here despite Dr. Windle's emphasis on the output, or change in motor activity. Spontaneous activity and *in utero* activity induced by sound or change of position may be important developmental components, but, still, at the time of birth, the afferent input is changed drastically. I think this is something that should not be avoided in discussing the change in fetal activity at birth.

*Windle:* Very good. Just this difference may be measured chemically.

*Pribram:* Why does the biochemist study whole brain?

*Roberts:* The biochemist doesn't always study whole brain because, as you will recall, Lowry (45), Hydén (29), Pope (60), and others have studied chemical properties of single neurons or small neuron groups and even parts of neurons.

*Leake:* But there is another aspect. A study of the chemicals that are in specific cells or aggregates of cells in the brain can be made by various techniques, and this will give some idea of the chemical pattern that exists within those cells or cellular aggregates. On the other hand, a study of the products of their metabolic interchange and measurement of those variations as they may occur in connection with the functional activity of the brain can also be made.

For instance, I was very impressed, when I was in the USSR, by experiments on the variations in the ammonia content of the brain as a result of over-all body activity. For example, if a resting rat is dropped into liquid air and frozen, and then its brain is removed and analyzed, a baseline for resting ammonia content of the brain can be obtained. If an animal is put into activity by working in a maze, which is what I saw, and then at the end of the maze dropped into liquid air, and its brain analyzed for ammonia, it will be found that there is an increase in the ammonia content, representing, then, an end product of over-all metabolic activity. This is another way by which the chemical processes, at any rate within the brain, may be guessed at, and it gives some kind of insight as to what may be involved in turnover.

*Roberts:* One can't analyze single cells for a component until one knows it is there. Usually, one must start with the bulk process and work down. One knows what enzymes to look for in a single neuron, because somebody has ground up a big piece of muscle, liver, kidney, or brain at one time or another, extracted it, purified an enzyme, studied its properties, and proved that this enzyme had a place in a certain metabolic sequence. It may be conjectured, for example, that the activity of this enzyme might be the rate-limiting factor in over-all rate at which glucose is broken down to pyruvic acid, and a properly performed measurement might give some hints about it. With sufficient ingenuity, the measurement eventually may be performed on single neurons or parts of neurons. The ability to do this and the need for performing such a determination has come as a part of the evolution of biochemical knowledge. One just doesn't go directly to the single cell or the cell nucleus.

Furthermore, there is always the question of how much more meaningful it is in functional terms if a variable is studied in a thousand single neurons than if functionally related cell masses are examined. This is a serious strategic problem which must be evaluated in terms of the goal which one hopes to achieve.

*Leake:* The analogy with muscle is good, because of the characteristics involved in what we call firing in respect to the neuron, which can be thought of as analogous to the sudden contraction of the muscle fiber. But there is another aspect to it in the brain; that is, there are pulsating cells in the brain. The oligodendroglia pulsate, showing a systole, as it were, of about 30 seconds in actual time, and a diastole of about 3.5 minutes. The Schwann cells and astrocytes also pulsate.

These activities can be followed by phase contrast microscopy and by time-lapse movies, so that one has a record. The phase contrast microscopy in itself gives some idea of the distribution of chemical elements with respect to at least fat and water; so that the development of this type of technique may also yield important chemical knowledge regarding the activity of the brain. But the point I was making is that the analogy with muscle is a pertinent one.

*Fremont-Smith:* And those oligodendroglia, if I understand it correctly, are also operating in the process of making one of the lipids, the myelin sheath, so that you now have a relationship between your pulsation and your lipids.

*Leake:* Yes. The work of Dr. Charles M. Pomerat, it seems to me, deserves attention (57,58,59).

*Windle:* You are making assumptions, of course, that conditions in the brain are similar to those in the test tube. We don't know that they are. Another assumption you are making is that there are only these specific categories of cells. There are probably many more. I doubt that there is a single type of oligodendrocyte. I think there are several cells that we now lump under the term, *oligodendrocyte.* We know that some have a relationship to the axis cylinders of nerve fibers and, at least in development, appear to be related to the formation of the myelin sheath. Others have a close relationship to capillaries in the gray matter and, from their structural arrangement, would seem to have some control over the blood that passes from the capillaries to nerve cells.

In all this, we, as cytologists, are making assumptions, just as the biochemists make assumptions on the basis of mixtures from a homogenizer.

*Leake:* We make another assumption; namely, that the homogenizer stops homogenizing at some stage, and we believe that the macromolecules that comprise the enzymes are not themselves broken up by the homogenizing process. Is there any information as to how finely the homogenizer actually does break up the components of the cells of the brain?

*Roberts:* I think there is some. People have worked out the tightness of the homogenizer necessary to homogenize just enough so one can centrifuge out morphologically good nuclei or isolate identifiable mitochondria, etc. Some workers are very artistic at this. By making the proper smears and staining or by using the electron microscope on the preparations, they can determine whether or not a homogenizer fits their purpose.

*Leake:* You get into difficulties of organizational levels in biological systems. When macromolecules are being dealt with, that is one level, and when macromolecules are aggregated into a cell, that is another level. We have as yet no justification for jumping from the findings at one level to those at another, unless global terms, which then are very indefinite, are used. I think that one of our great needs is to try to find some of the factors that are involved in the Gestalt at different levels.

*Bridger:* This discussion on levels of organization and the remarks about C. Judson Herrick remind me of a contribution that Herrick (26) made to this problem in "A Biological Survey of Integrative Levels."

*Leese:* I think that Dr. Leake has brought out an interesting point in relation to the Gestalt at different levels. Makarov (49) has suggested a reconsideration of cellular function in terms of Gestalt at this level. He has referred to the functions ascribed to different cellular fractions such as the cytoplasm, nucleus, nucleolus, etc., and has called attention to the confusion which exists pertaining to biochemical organization and cytological function upon which Dr. Roberts has remarked. Makarov has indicated that in the manifestations of life activity, even at this first level, we should consider, not the individual components, but the cell as a whole.

*Roberts:* I realize that one of our problems is in understanding the really technical details of the sciences that are on the borderline of our own, with which we try to integrate our findings and concepts. I think that is much more important than exchange of philosophy. The tightness of the homogenizer sometimes may be much more important than understanding some basic philosophic concept, for the time being, for the solution or understanding of a particular problem. For example, if a neurophysiologist were to try to incorporate the results of improperly conducted or interpreted results of experiments on glycolysis and respiration of nervous tissue performed by someone else into an explanation of some electrical phenomena which he himself has observed, he would be weakening his position greatly. This is why I think that the understanding of experimental details and techniques is so important. A person who wants to assess the role of lipids in regulating ion permeabilities in neurons must know the structures of the lipids which are present and the physical states in which they exist. Otherwise, his work will be meaningless in molecular terms. I feel that the great generalizations come from a profound understanding of detail.

*Fremont-Smith:* It seems to me that if you follow your point of view all the way, you are saying that everyone should wait and not think until all the details are in. This is obviously not what has been done. The whole advancement of science has come by using data at a certain stage of development for a new conceptualization. At the present time, since the rate of precise development in each area is so very rapid and is progressively increasing in rapidity, we literally cannot catch up with what is going on even in any one area. There are more than thirty thousand journals published every month in biology and medicine alone. If we were to take any particular area and decide that we would really cover the literature in it, we might never be able to keep up with it because it is coming out too fast, even with a mechanical aid for retrieving data.

It seems to me, therefore, that we must do what we have always done, *i.e.*, work with incomplete data and incomplete concepts, recognizing that they are probably going to be proved to be more or less fallacious, and that we shall have to build new ones. But they may provide a new frame of reference to stir another group of people to move in a different direction.

*Bodian:* May I assert that the homogenizer contains an important generalization. This is that, at this level of grinding, there is a significant set of cellular organelles to be isolated for study. Those generalizations which lead to progress are often related directly to the method of examining the thing we are studying. They are operational. I assume that in this discussion Dr. Roberts is primarily concerned with generalizations which are experiment-oriented and Dr Fremont-Smith is emphasizing the importance of "free-floating" generalizations which go beyond the data, and beyond the method.

*Pribram:* There is another point, though, which I would like to come back to, and that is philosophy. I think the techniques we have for relating methods must be as precise as the methods themselves. The homogenizer was a good example of a very important specific point on methods. If we are going to that level of detail, then we must also apply it to the relations between methods. Techniques for interrelating methods can be equally precise, *e.g.*, mathematical set theory. Such mathematical ways of expressing relationships offer considerably more than does vague talk of inhibition and release from inhibition. Is the inhibition concerned to be at a cellular level, or at the level of organ systems, or of the total organism? These concepts are used so loosely that one has no business talking about the size of the homogenate at the same time.

*Leake:* There is another point of very great importance, and that is the significance of a basic philosophical approach. In our field, this was made, I think, around 1847, largely by Emil Du Bois-Reymond, Hermann von Helmholtz, and Carl Ludwig, when they announced, as an article of faith, that all living processes, including consciousness or the functioning of memory or any other aspect of brain activity, are explainable in terms of physics and chemistry (10). This was taken up and incorporated very significantly, it seems to me, in the whole Russian approach, and it is assumed, in general, in our own approach.

Here, for example, in connection with the matter of enzyme activity and the inhibition factor that you brought up, what is involved primarily, we think, is the matter of energy exchange. We are concerned primarily with the storage of energy in living materials in our brain cells, with the transport of energy by some kind of molecules or other, and by the exchange of energy between one molecule and another.

*Pribram:* No. I think that is just the kind of thing that we're *not* concerned with. We are concerned with the organization of energy and the meaning of the organization of those patterns. If we go to the level of the central nervous system and talk about energy exchanges and quantitative relationships between amounts of energy, we're just at the wrong level of discourse. We're talking here about information and control processes, not energy exchanges *per se*.

*Leake:* Yes, but isn't it just these interchanges of quantity of energy, the absorption of them by one molecule, in contrast to absorption by another, that brings about the change in the molecular configuration or brings about the change in the chemical reaction?

*Pribram:* At such a minute level that it is trivial by comparison with the total energy changes that are taking place. The vacuum tube is the best analogy that comes to mind, and is familiar to all of us. By measuring the potential difference between input and output across the power supply of the tube, one learns very little about what the vacuum tube can do. Basically, the tube is a control mechanism whose output is programmed by what goes on at the grid, and this is determined by very minute changes of energy. So, if one takes the whole brain and measures the changes in energetics going on, one learns practically nothing about its critically important functions which are to organize energy and control it.

*Bodian:* Yes. In relation to what you said, it seems interesting that the problem of the cell, as the geneticist and cytogeneticist see it, is analogous to the problem of the brain; that is, we are dealing with information processing and the transmission of information, and the processing is the limiting factor and not the energy. Although the cell faces problems of information processing at a totally different level from that which the brain faces, there may be parallels at these two levels of information transfer, and if so we shall have to study enzymes as well as higher levels of organization to achieve a reasonably complete picture.

*Roberts:* One of the problems I have been facing relates to neurophysiology. It is obvious to me, now, that even if I were to read nothing but the literature in neurophysiology for some time, I couldn't really understand and have the feeling for neurophysiology that one who is practicing it does. The only answer that I can see, and this is probably trite since I am sure many people have said similar things, is to have people who are great experts in neurophysiology, biochemistry, and related areas working in sufficiently close proximity so that a *voluntary* overlap of activity and discussion occurs. In such an environment, the latest and best thinking in each field would be represented. Then an expert in one field would not need to read and evaluate all of the literature in another, but could maintain a considerable sophistication, intellectually and technically, through his contact with specialists in other fields. In such areas of overlap integrations can develop.

*Fremont-Smith:* That is the purpose of a Macy conference—to help us gain knowledge of and confidence in each other's concepts. I think this discussion shows how necessary it is to do this. The very fact that we would spend half an hour discussing this is an indication of the real need of more exchange between the overlapping human computing machines, such as we have in this room now.

## REFERENCES

1. ALBERS, R. W.: Gamma-aminobutyric acid. *In the Neurochemistry of Nucleotides and Amino Acids*. R. O. Brady and D. B. Tower, Eds. New York, John Wiley & Sons, 1960 (pp. 146-153).
2. AXELSSON, J., and THESLEFF, S.: A study of supersensitivity in denervated mammalian skeletal muscle. *J. Physiol.* **147**, *178-193 (1959)*.
3. BAXTER, C. F., and ROBERTS, E.: Elevation of $\gamma$-aminobutyric acid in rat brain with hydroxylamine. *Proc. Soc. Exper. Biol. & Med.* **101**, *811-815 (1959)*.
4. ———: Demonstration of thiosemicarbazide-induced convulsions in rats with elevated brain levels of $\gamma$-aminobutyric acid. *Proc. Soc. Exper. Biol. & Med.* (In press).
5. BAXTER, C. F., ROBERTS, E., and EIDELBERG, E.: $\gamma$-Aminobutyric acid and seizure susceptibility in areas of normal cat brain cortex. *J. Neurochem.* **5**, *203-205 (1960)*.
6. BAXTER, C. F., SCHADÉ, J. P., and ROBERTS, E.: Maturational changes in cerebral cortex. II. Levels of glutamic acid decarboxylase, gamma-aminobutyric acid and some related amino acids. *Inhibition in the Nervous System and $\gamma$-Aminobutyric Acid*. E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 214).
7. BODIAN, D.: Nucleic acid in nerve-cell regeneration. *Symp. Soc. Exper. Biol.* **1**, *163-178 (1947)*.
8. BRADY, R. O., SPYROPOULOS, C. S., and TASAKI, I.: Intra-axonal injection of biologically active materials. *Am. J. Physiol.* **194**, *207-213 (1958)*.
9. CHANCE, B.: A digital computer representation of chemical and spectroscopic studies on chemical control of ascites tumor cell metabolism. *In Amino Acids, Proteins and Cancer Biochemistry*. J. T. Edsall, Ed. New York, Academic Press, 1960 (pp. 191-212).
10. CRANEFIELD, P. F.: The organic physics of 1847 and the biophysics of today. *J. Hist. Med. & Allied Sc.* **12**, *407-423 (1957)*.
11. CUAJUNCO, F.: Embryology of the neuromuscular spindle. *Contrib. Embryol. (Carnegie Inst.)* **19** *(No. 99), 45-72 (1927)*.
12. CURTIS, D. R., and WATKINS, J. C.: Investigations upon the possible synaptic transmitter function of gamma-aminobutyric acid and naturally-occurring amino acids. *Inhibition in the Nervous System and $\gamma$-Aminobutyric Acid*. E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 424).
13. DANILOVA, N. N.: The driving response of human brain to stimulation with flickers close to alpha-rhythm frequency in the course of the development of sleep inhibition. *Problems of Electrophysiology and Electroencephalography*. The Works of the 1st All-Union Conference. Leningrad, 8-13 May 1957, Moscow-Leningrad, 1960. (In Russian).
14. DIAMOND, J., and MELEDI, R.: The sensitivity of foetal and newborn rat muscle to acetylcholine. *J. Physiol.* **149**, *50P (1959)*.

15. Doty, R. W., and Gerard, R. W.: Nerve conduction without increased oxygen consumption: action of azide and fluoroacetate. *Am. J. Physiol.* **162,** *458-468 (1950).*
16. Dunlop, C. W., Adey, W. R., Killam, K. F., and Brazier, M. A. B.: Mechanism of action of thiosemicarbazide and metrazol on cerebellar and cerebral activity in the cat. *Am. J. Physiol.* 198, *399-404 (1960).*
17. Eidelberg, E., Baxter, C. F., Roberts, E., Saldias, C. A., and French, J. D.: Anticonvulsant properties of hydroxylamine and elevation of cerebral γ-aminobutyric acid in cats. *Proc. Soc. Exper. Biol. & Med.* **101,** *815-817 (1959).*
18. Eyzaguirre, C.: The electrical activity of mammalian intrafusal fibers. *J. Physiol.* **150,** *169-185 (1960).*
19. Flexner, L. B.: Enzymatic and functional patterns of the developing mammalian brain. *In Biochemistry of the Developing Nervous System.* H. Waelsch, Ed. New York, Academic Press, 1955 (pp. 281-300).
20. Flexner, J. B., Flexner, L. B., and Straus, W. L., Jr.: The oxygen consumption, cytochrome and cytochrome oxidase activity and histological structure of the developing cerebral cortex of the fetal pig. *J. Cell. & Comp. Physiol.* **18,** *355-368 (1941).*
21. Florey, E.: Evidence for Factor I containing neurons in mammalian central nervous system. *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 202).
22. Florey, E., and Biederman, M. A.: Studies on the distribution of Factor I and acetylcholine in crustacean peripheral nerve. *J. Gen. Physiol.* **43,** *509-522 (1960).*
23. Fox, D. L.: *Animal Biochromes and Structural Colours.* New York, Cambridge Univ. Press, 1953.
24. Gordon, M. W.: Role of adaptive enzyme formation in morphogenesis. In: *Progress in Neurobiology.* Vol. I, Chapt. VII. S. R. Korey, and J. I. Nurnberger, Eds. New York, Hoeber-Harper, 1956 (pp. 83-100).
25. Granit, R., Skoglund, S., and Thesleff, S.: Activation of muscle spindles by succinylcholine and decamethonium. Effects of curare. *Acta physiol. scandinav.* **28,** *134-151 (1953).*
26. Herrick, C. J.: *Philosophy for the Future.* Sellars, McGill, and Farber, Eds. New York, Macmillan, 1949.
27. Hess, E. H.: Imprinting. An effect of early experience, imprinting determines later social behavior in animals. *Science* **130,** *133-141 (1959).*
28. Howe, H. A., and Mellors, R. C.: Cytochrome oxidase in normal and regenerating neurons. *J. Exper. Med.* **81,** *489-500 (1945).*
29. Hydén, H.: Biochemical changes in glial cells and nerve cells at varying activity. In: *Proc. IV Internat. Congr. Biochem. Vol. III, Biochemistry of the Central Nervous System.* F. Brücke, Ed. London, Pergamon Press, 1959 (pp. 64-89).

*30. Kasatkin, N. I.: Early conditional reflexes in the child. *Pavlov Higher Nerv. Act.* 2 *(No. 4), 572-581 (1952).*

*31. Khudorozheva, A. T.: The role of the cerebellum in the development of the functions of skeletal muscles in ontogenesis. *Material on Evolutionary Physiology. (No. 1), 333-348 (1956).* (In Russian)

32. Kishimoto, Y., and Radin, N. S.: Composition of cerebroside acids as a function of age. *J. Lipid Res.* 1, *79-82 (1959).*

33. Klüver, H.: On naturally occurring porphyrins in central nervous system. *Science* 99, *482-484 (1944).*

34. ———: Porphyrins, nervous system, and behavior. *J. Psychol.* 17, *209-228 (1944).*

35. ———: Functional differences between the occipital and temporal lobes. In: *Cerebral Mechanisms in Behavior.* L. A. Jeffress, Ed. New York, John Wiley & Sons, 1951 (pp. 147-182).

36. ———: Porphyrins in relation to the development of the nervous system. In: *Biochemistry of the Developing Nervous System.* H. Waelsch, Ed. New York, Academic Press, 1955 (pp. 137-144).

37. Knox, W. E., Auerbach, V. H., and Lin, E. C. C.: Enzymatic and metabolic adaptations in animals. *Physiol. Rev.* 36, *164-254 (1956).*

38. Kuffler, S. W., and Edwards, C.: Mechanism of gamma aminobutyric acid (GABA) action and its relation to synaptic inhibition. *J. Neurophysiol.* 21, *589-610 (1958).*

39. Kuhlman, R. E., and Lowry, O. H.: Quantitative histochemical changes during the development of the rat cerebral cortex. *J. Neurochem.* 1, *173-180 (1956).*

40. Lajtha, A., Berl, S., and Waelsch, H.: Compartmentalization of glutamic acid metabolism in the central nervous system. *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 460).

41. Langworthy, O. R.: Correlated physiological and morphological studies of the development of the electrically responsive areas in the cerebral cortex of the opossum. *Contrib. Embryol. (Carnegie Inst.)* 19 *(No. 103), 149-176 (1927).*

42. Lindsley, D. B.: Heart and brain potentials of human fetuses *in utero. Am. J. Psychol.* 55, *412-416 (1942).*

43. ———: The reticular system and perceptual discrimination. In: *Reticular Formation of the Brain.* Boston, Little, Brown, 1958 (pp. 513-534).

44. Lowe, I. P., Robins, E., and Eyerman, G. S.: The fluorimetric measurement of glutamic decarboxylase and its distribution in brain. *J. Neurochem.* 3, *8-18 (1958).*

45. Lowry, O. H.: Enzyme concentrations in individual nerve cell bodies. In: *Metabolism of the Nervous System.* (2nd Internat. Neurochem. Symp., Aarhaus, Denmark, 1956) D. Richter, Ed. London, Pergamon Press, 1957 (pp. 323-328).

46. Luria, A. R., and Yudovich, F. I.: *Speech and the Development of Mental Processes in the Child.* London, Staples Press, 1959.
47. McCormick, D. B., and Snell, E. E.: Pyridoxal kinase of human brain and its inhibition by hydrazine derivatives. *Proc. Nat. Acad. Sc.* **45**, *1371-1379 (1959).*
48. McKhann, G. M., Albers, R. S., Sokoloff, L., Mickelsen, O., and Tower, D. B.: The quantitative significance of the gamma-aminobutyric acid pathway in cerebral oxidative metabolism. *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 169).

*49. Makarov, P. V.: Recent data on the structure and properties of the cell nucleus. *Archives of Anatomy, Histology, and Embryology.* **35** *(No. 6), 3-21 (1958).*

50. Moog, F.: The differentiation of enzymes in relation to the functional activities of the developing embryo. *Ann. New York Acad. Sc.* **55,** *57-66 (1952).*
51. Needham, J.: *Chemical Embryology.* Cambridge, Univ. Press, 1931.
52. Pardee, A. B., Jacob, F., and Monod, J.: The genetic control and cytoplasmic expression of "inducibility" in the synthesis of β-galactosidase by *E. coli. J. Mol. Biol.* **1,** *165-178 (1959).*
53. Peters, J. J., Vonderahe, A. R., and Powers, T. H.: The functional chronology in developing chick nervous system. *J. Exper. Zool.* **133,** *505-518 (1956).*
54. Peters, V. B., and Flexner, L. B.: Biochemcial and physiological differentiation during morphogenesis; quantitative morphologic studies on developing cerebral cortex of the fetal guinea pig. *Am. J. Anat.* **86,** *133-161 (1950).*
55. Petrushka, E., and Giuditta, A.: Electron microscopy of two subcellular fractions isolated from cerebral cortex homogenate. *J. Biophys. et Biochem. Cytol.* **6,** *129-131 (1959).*
56. Pisano, J. J., Wilson, J. D., Cohen, L., and Udenfriend, S.: Occurrence of a compound in brain containing γ-aminobutyric acid and histidine. *Fed. Proc.* **19,** *334 (1960).*
57. Pomerat, C. M.: Pulsatile activity of cells from the human brain in tissue culture. *J. Nerv. & Ment. Dis.* **114,** *430-449 (1951).*
58. ———: Dynamic neurogliology. *Texas Rep. Biol. & Med.* **10,** *885-913 (1952).*
59. ———: Rotating nuclei in tissue cultures of adult human nasal mucosa. *Exper. Cell. Res.* **5,** *191-196 (1953).*
60. Pope, A., Hess, H. H., and Allen, J. N.: Quantitative histochemistry of proteolytic and oxidative enzymes in human cerebral cortex and brain tumors. In: *Progress in Neurobiology.* Vol. II., H. Waelsch, Ed. New York, Hoeber-Harper, 1957 (p. 182-194).
61. Purpura, D. P.: Origin of cortical surface potentials. *Neuropharmacology.* H. A. Abramson, Ed. Trans. Third Conf. New York, Josiah Macy, Jr. Foundation, 1957 (pp. 297-322).

62. ———: Pharmacological action of ω-amino acid drugs on different cortical synaptic organizations. *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (pp. 495-515).

63. Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Succinylcholine-induced contractures in skeletal muscles of newborn cat. *Proc. Soc. Exper. Biol. & Med.* **103**, *336-338 (1960).*

64. Purpura, D. P., Girado, M., Smith, T. G., Callan, D. A., and Grundfest, H.: Structure-activity determinants of pharmacological effects of amino acids and related compounds on central synapses. *J. Neurochem.* **3**, *238-268 (1959).*

65. Purpura, D. P., Girado, M., Smith, T. G. Jr., and Gomez, J. A.: Effects of systemically administered ω-amino and guanidino acids on spontaneous and evoked cortical activity in regions of blood-brain barrier destruction. *EEG Clin. Neurophysiol.* **10**, *677-685 (1958).*

66. Roberts, E. (Ed.): *Inhibition in the Nervous System and γ-Aminobutyric Acid.* Oxford, Pergamon Press, 1960.

67. Roberts, E., Baxter, C. F., and Eidelberg, E.: Some aspects of cerebral metabolism and physiology of γ-aminobutyric acid. *Function and Structure of the Cerebral Cortex.* J. P. Schadé, Ed. Amsterdam, Elsevier Press. (In press).

68. Roberts, E., and Frankel, S.: Further studies of glutamic acid decarboxylase in brain. *J. Biol. Chem.* **190**, *505-512 (1951).*

69. Roberts, E., Frankel, S., and Harman, P. J.: Amino acids of nervous tissue. *Proc. Soc. Exper. Biol. & Med.* **74**, *383-387 (1950).*

70. Roberts, E., Harman, P. J., and Frankel, S.: γ-aminobutyric acid content and glutamic decarboxylase activity in developing mouse brain. *Proc. Soc. Exper. Biol. & Med.* **78**, *799-803 (1951).*

71. Roberts, E., Lowe, I. P., Guth, L., and Jelinek, B.: Distribution of γ-aminobutyric acid and other amino acids in nervous tissue of various species. *J. Exper. Zool.* **138**, *313-328 (1958).*

72. Roberts, E., Rothstein, M., and Baxter, C. F.: Some metabolic studies of γ-aminobutyric acid. *Proc. Soc. Exper. Biol. & Med.* **97**, *796-802 (1958).*

73. Schadé, J. P., and Baxter, C. F.: Changes during growth in the volume and surface area of cortical neurons in the rabbit. *Exper. Neurol.* **2**, *158-178 (1960).*

74. Schwerin, P., Bessman, S. P., and Waelsch, H.: The uptake of glutamic acid and glutamine by brain and other tissues of the rat and mouse. *J. Biol. Chem.* **184**, *37-44 (1950).*

75. Shen, S. C.: Enzyme development as ontogeny of specific proteins. In: *Biological Specificity and Growth.* (Society for the Study of Development and Growth Symp. No. 12.) E. G. Butler, Ed. Princeton, Princeton Univ. Press, 1955 (pp. 73-92).

76. Sisken, B., Roberts, E., and Baxter, C. F.: Gamma-aminobutyric acid and glutamic decarboxylase activity in the brain of the chick. *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 219).
77. Smith, K. C., Cordes, E., and Schweet, R. S.: Fractionation of transfer ribonucleic acid. *Biochim. et biophys. acta* 33, *286-287 (1959).*
78. Sokolov, E. N.: The representation of the orienting reflex in the EEG in human subjects. The problems of electrophysiology and electroencephalography. *Proc. 1st All-Union Conference on Problems Connected with the Electrophysiology of the Central Nervous System*, (May 8-11, 1957). Leningrad, Academy of Sciences, USSR, 1957. (In Russian).
79. ———: Concerning the reflection of the orienting response in the EEG of man. *Problems of Electrophysiology and Electroencephalography.* Proc. of the 1st All-Union Conference. Leningrad, May 8-11, 1957, Moscow-Leningrad, 1960. (In Russian).
80. Sperry, R. W.: Physiological plasticity and brain circuit theory. In: *Biological and Biochemical Bases of Behavior.* H. F. Harlow and C. N. Woolsey, Eds. Madison, Univ. of Wisconsin Press, 1958 (pp. 401-424).
81. Szilard, L.: The control of the formation of specific proteins in bacteria and in animal cells. *Proc. Nat. Acad. Sc. (USA)* 46, *277-292 (1960).*
82. ———: The molecular basis of antibody formation. *Proc. Nat. Acad. Sc. (USA)* 46, *293-302 (1960).*
83. Terzuolo, C. A., Sigg, B., and Killam, K. F.: Effect of thiosemicarbazide on responses of spinal motoneuron. In: *Inhibition in the Nervous System and γ-Aminobutyric Acid.* E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 336).
84. Van Gelder, N. M., and Elliott, K. A. C.: Disposition of γ-aminobutyric acid administered to animals. *J. Neurochem.* 3, *139-143 (1958).*
85. Varga, E., Kövér, A., Kovács, T., and Hetényi, E.: Changes in cholinesterase activity of striated muscle after denervation. *Acta physiol. acad. sc. Hung.* 11, *235-242 (1957).*

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*An English translation of the papers starred is included in *The Central Nervous System and Behavior: Selected Translations from the Russian Medical Literature* (1960), which was precirculated to members of the conference by the U. S. Department of Health, Education, and Welfare and distributed to medical schools in the U. S. and Canada.

# NEURONAL MODELS AND THE ORIENTING REFLEX

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I WOULD LIKE TO PROPOSE four general problems for discussion: the objective study of sensory integration; the components of the orienting reflex; the neuronal model and the structure of the orienting reflex; and the application of the neuronal model to the explanation of the conditional reflex.

One of the most important tasks of the central nervous system, according to Adrian (2), is sensory integration. By sensory integration is understood the process by which individual stimuli become integrated into a pattern which, as a whole, determines the responses of animals and man. The Gestalt psychologists, for example Koffka (35), emphasized the important role of the relationship between elements in a complex, but the data obtained in the subjective observations were very difficult to explain in physiological terms. With the development of Pavlovian theory, the application of objective methods to the study of sensory integration became possible. This method was based on the elaboration of conditional reflexes that are differential to complex and single stimuli (28,29,78,79).

Pavlov himself declared that there were two different ways by which the nervous system can discriminate impulses: The first is the excitatory process which starts when the orienting reflex is initiated by a change of stimulation, and the second is the elaboration of different reflexes, positive and negative. The second is the more complex because the afferent integration and differentiation of stimuli are elaborated through the development of inhibitory and excitatory processes in two different motor reflexes. Use of the orienting reflex is the simpler method for evaluating sensory integration and sensory analysis and is more direct than the use of conditional reflexes, for the orienting reflex antecedes the elaboration of differential conditional reflexes.

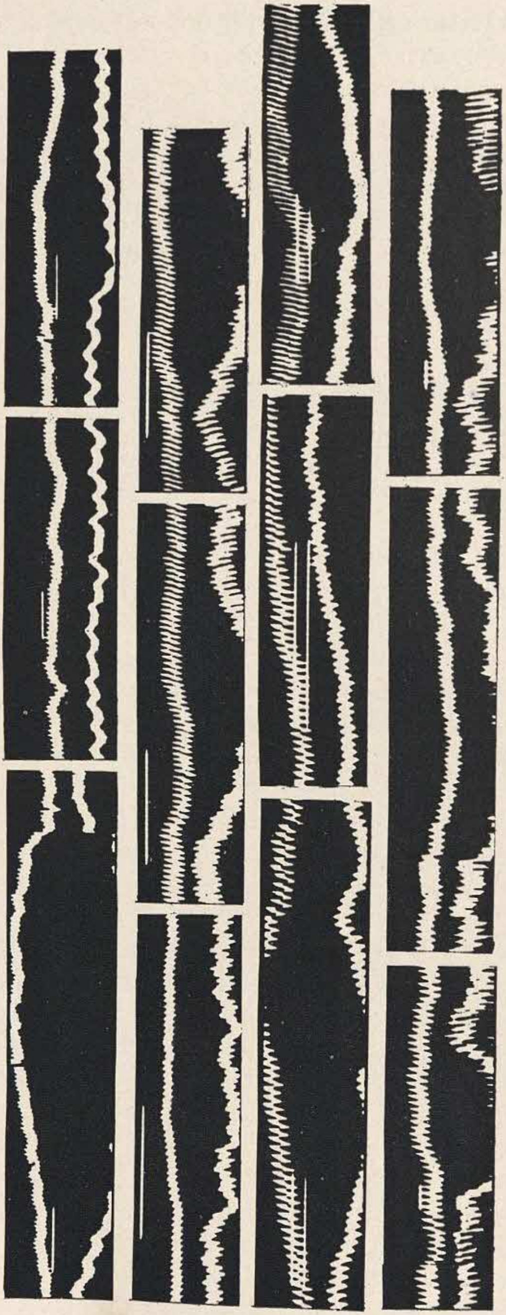

FIGURE 85. Orienting, adaptive, and defensive reflexes in man. Each upper trace represents vascular response in the head, and each lower trace vascular response in the finger. Upward deflections: vasodilation. Downward deflections: vasoconstriction. Horizontal lines = presentation of stimulus. (*A*) SOUND: Left, orienting response to new stimulus. Center, habituation on repetition. Right, recovery of orienting reflex to sound after external stimulation. (*B*) COLD: Left, nonspecific orienting response. Center, specific adaptive response with vasoconstriction in both head and finger. Right, return of nonspecific orienting response after external stimulation. (*C*) WARMTH: Left, nonspecific orienting response. Center, specific adaptive vasodilation in both head and finger. Right, recovery of orienting response to warmth after external stimulation. (*D*) ELECTRIC SHOCK: Left, orienting response. Center, defensive reflex. Right, recovery of orienting response to shock after external stimulation.

The term *orienting reflex* was introduced by Pavlov in 1910 (43,44). This reflex is characterized by two general properties: The first is that it is an unspecific reflex and is initiated by any increase, decrease, or qualitative change of a stimulus, independent of the modality of the stimulating agent. The second property is that it is subject to extinction or habituation on repeated presentation. This orienting reflex is a special functional system which can be differentiated from the other two general types of unconditioned reflexes—the adaptive reflex and the defensive reflex. The adaptive reflex is the reflex connected with the direction of a change of stimulus, and the defensive reflex is a general response of the organism when the stimulus is too strong for normal functioning.

For example, when we record the vascular response of the vessels of the head and of the finger simultaneously, as in Figure 85, we find with the orienting reflex, whether evoked by sound *A*, cold *B*, warmth *C*, or electrical shock *D*, that there is dilation of the vessels of the head and a simultaneous vasoconstriction of the vessels of the finger.

This reaction, and this is the important point, is produced only by the first few presentations of the stimuli. The response is unspecific, *i.e.*, irrespective of the modality of stimulation. This is a sign of the orienting reflex. For example, after ten or fifteen presentations (Figure 85 *A*, center record), sound no longer produced an effect. Cold produced the adaptive reflex in the form of vasoconstriction in head and hand (*B*, center record). Warmth also produced a specific adaptive reflex but in the form of vasodilation in both head and hand (*C*, center record). Shock produced a special defensive reflex (*D*, center record).

When we aroused the subject by an additional loud sound, he could be brought back to the first stage of nonspecific orienting reflexes. Once again, sound, cold, warmth, and shock produced the same nonspecific effect. We can, therefore, differentiate the orienting nonspecific reflex (which can be extinguished) from the specific adaptive reflex, which is persistent in spite of repeated presentations. We can differentiate a defensive reflex, which is also stable in spite of repeated presentations (77).

Two different forms of orienting reflex can be distinguished: a generalized orienting and a localized orienting reflex. When we record simultaneously the occipital EEG, the EEG of the motor region, the skin galvanic response (SGR), muscle tension, eye movements, and respiration, the first presentation of tactile stimulation produces a generalized response (Figure 86).

After twenty-four presentations, the only effect is a slight depression of EEG in the motor region. The other components are inhibited.

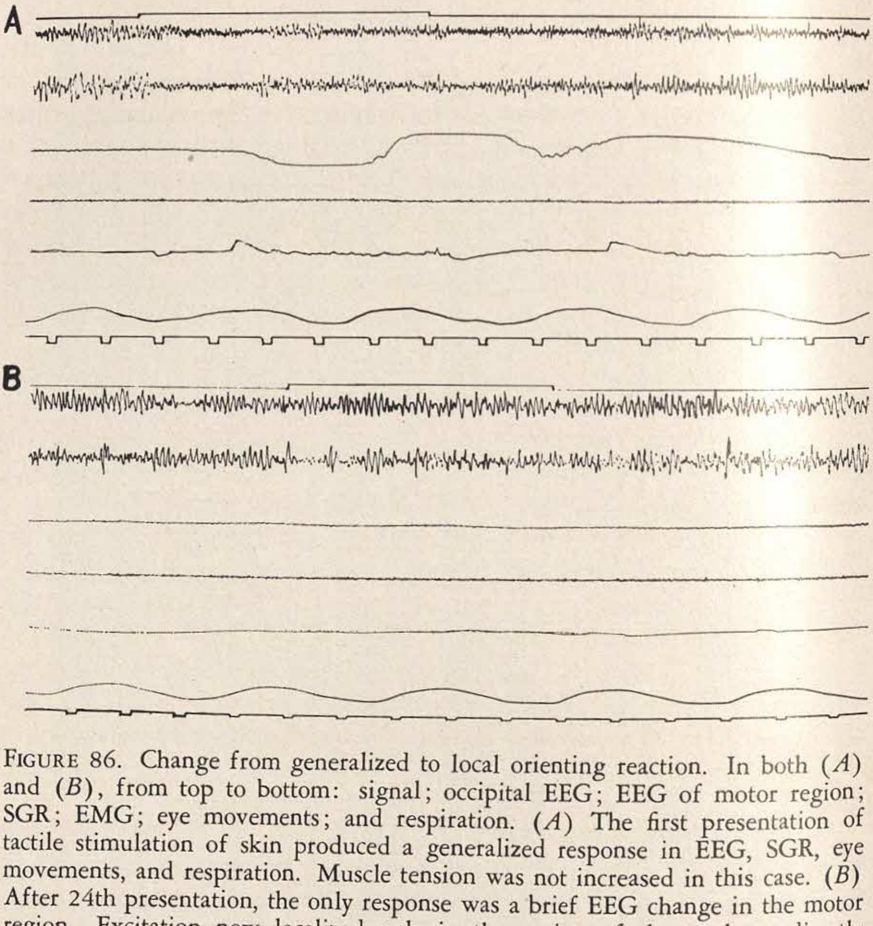

FIGURE 86. Change from generalized to local orienting reaction. In both (*A*) and (*B*), from top to bottom: signal; occipital EEG; EEG of motor region; SGR; EMG; eye movements; and respiration. (*A*) The first presentation of tactile stimulation of skin produced a generalized response in EEG, SGR, eye movements, and respiration. Muscle tension was not increased in this case. (*B*) After 24th presentation, the only response was a brief EEG change in the motor region. Excitation now localized only in the region of the analyzer directly stimulated.

Therefore, during the course of repeated presentations, the generalized form of the orienting response, which includes a different analyzer system, changes into a local form, which is a kind of activation of the specific analyzer that is being stimulated.

It is important to recognize that the localized form of the orienting reaction in some degree became related to the modality of stimulation. If I use tactile stimulation or a change in proprioceptive stimuli, there is a localized response in the motor region. If I use light, the special localized response appears in the occipital EEG and in specific eye movements. The result depends on the modality of stimulation.

*Leese:* Did you say that the orienting reflex is very quickly extinguished?

*Sokolov:* The generalized form can be extinguished after ten or fifteen presentations, but the local form only after twenty-five or thirty presentations, or even more.

*Keller:* The orienting reflex is the same as the unconditioned reflex?

*Sokolov:* That's right. The orienting reflex is the unconditioned reflex, but it includes some conditional mechanism. I shall explain it later. The orienting reflex, which includes some vegetative, somatic, electroencephalographic, and sensory components, is a unitary system, and the role of these components is to increase the discriminatory power of analyzers.

Figure 87 shows a record of a man's reaction to repeated presenta-

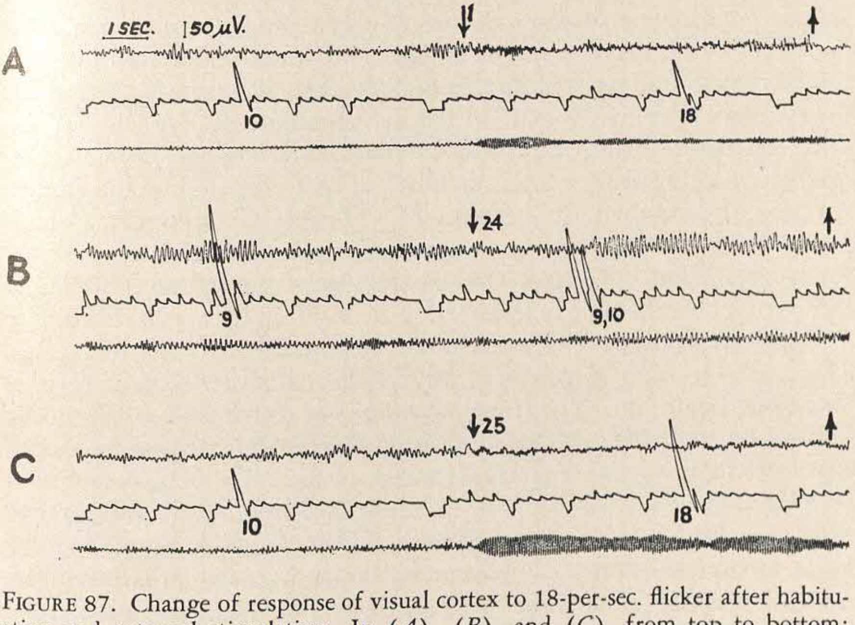

FIGURE 87. Change of response of visual cortex to 18-per-sec. flicker after habituation and external stimulation. In (*A*), (*B*), and (*C*), from top to bottom: occipital EEG, frequency analysis of EEG, and response of the 18-cps filter of analyzer. (*A*) Before flicker, EEG frequency was 10 cps. 1st presentation evoked EEG response at 18 cps, seen most precisely on the 18-cps filter. (*B*) 24th presentation (habituation): $\alpha$-rhythm has slowed to 9 cps. Flicker produces slight increase in frequency (*i.e.*, 10-cps peak in analyzer trace), but no response at 18 cps. (*C*) 25th presentation after auditory stimulation: $\alpha$-rhythm drops in amplitude. Same flicker at 18 per sec now produces strong driving with complete depression of $\alpha$-rhythm. The 18-cps filter reacts intensely.

tions of flashes of light at a frequency of 18 cps. The first line in each record indicates the EEG of the occipital region. The second line represents the frequency analysis by a Grey Walter analyzer over an epoch of 10 seconds. After twenty-three presentations, the same light produced a different response. The $\alpha$-rhythm changed from 10 cps to 9, and there was no response at the flicker rate (18 cps). This indicates that by habituation of the orienting reflex, the responsivity of the visual cortex is diminished.

Then, we stimulated the subject with a sound 70 db above threshold, 1000 cps, and after arousal, we presented the same flicker. The $\alpha$-rhythm was completely abolished during the light stimulation, and the response to 18 cps was increased. After the reinstatement of the orienting reflex, there was an increase of responsivity of the visual cortex.

The orienting reflex influences not only the central part of the visual system, but also the visual receptors. We have studied the responses in the rabbit by means of a special contact lens which is inserted into the eye, so that around the contact lens there is a special ring which prevents the eyes from closing. We can in this way stimulate the eye without any effect on the responses produced by mechanical change in the transmission of light between the lids. The pupils are dilated by the administration of atropine. The rabbit is in a plexiglass box, under a plexiglass saddle, so that its movements are minimized, but it is in a quite comfortable position. We have studied the electroretinogram (ERG) by means of a Grey Walter analyzer, the circuits of which we have changed so that frequencies from 1.5 cps to 480 cps can be selectively registered (Figure 88). The response of the retina to 30-per-second flash is shown in Figure 89. The uppermost trace of Figure 89 *B* shows the B-wave of the ERG with practically no detectable response to flicker, that is, without special frequency analysis of the ERG. The response of the filter adjusted to the frequency used for the stimulation indicates that, after a certain period of nonresponsivity, the retina responds increasingly to high-frequency stimulation as the stimulation proceeds. This method was first elaborated by Granit (25), and we have used it for the study of the ERG by high frequencies of flashes of light.

Under the influence of sound, which produces an orienting reflex, there is an increase of the ERG's response to high-frequency stimulation. At first, it seems strange that the peripheral part of the visual system can be influenced by arousal, but the work of Granit (25) and some other investigators has indicated the role of the reticular formation in the centrifugal control of peripheral sense organs and central parts of the

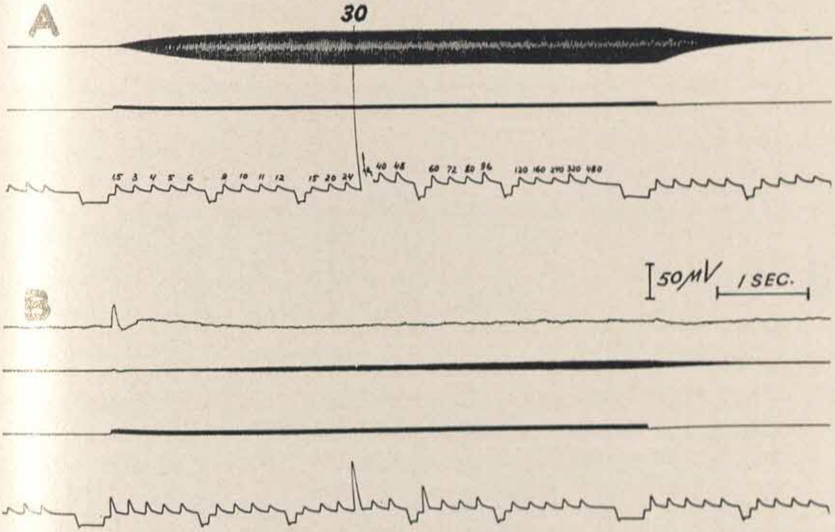

FIGURE 88. (*A*) Control: response of analyzer to flicker through photocell. Top trace: response of 30-cps filter. 2nd trace: response of the photocell. 3rd trace: frequency analysis of electrical current produced in photocell by flicker. The numbers indicate the selective frequencies of each filter from 1.5 to 480 cps (modification of Walter analyzer). Every filter adjusted so that a change of 1 cps produced a drop to an eighth of the response. (*B*) Analysis of ERG in a rabbit stimulated by flicker at 30 per sec. Top trace: B-wave of ERG. 2nd trace: response of filter. 3rd trace: response of photocell to flicker. 4th trace: frequency analysis of ERG.

analyzers as well. An example of the increase of the response of the eye to flashes of light with a frequency of 20 cps is given in the integrated responses shown in Figue 90. After the presentation of sound, evoking the orienting reflex, a certain increase of the response to 20 cps is seen. At the same time, the B-wave is not changed. This increase is connected only with the high-frequency stimulation.

Figure 91 shows superimposed oscillographic traces of the ERG response to 20-per-second flicker (*A* and *B*) and 5-per-second flicker (*C* and *D*) before and after arousal by sound. There is a marked increase in size of the ERG response in each case after the sound.

Under the influence of sound, the shape of the ERG is changed so that the highest point comes nearer to the onset of each flash. This means that the cycle of excitation in the ERG is shortened, and this is the mechanism for the increase of reaction to higher frequency demonstrated before. It also means that under the influence of sound, the

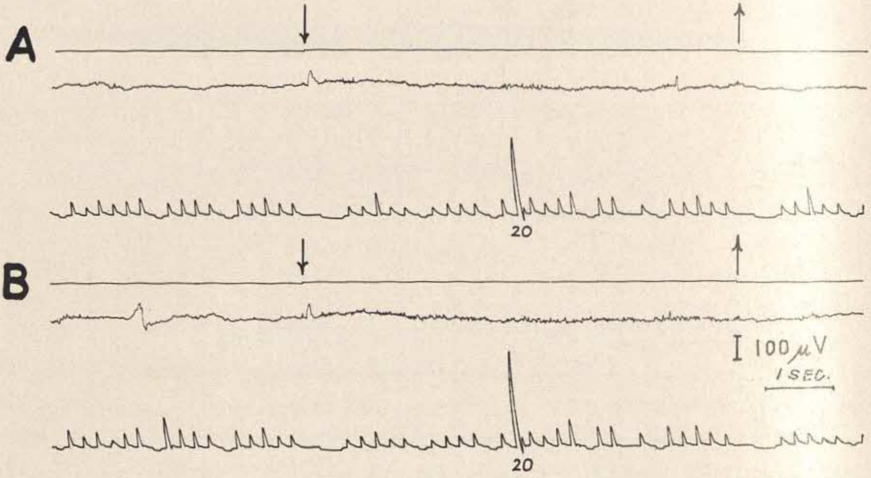

FIGURE 89. The increase of the ERG response to a 20-per-sec flicker after the acoustically evoked orienting reflex. In both (*A*) and (*B*), from top to bottom: signal, the ERG, and the frequency analysis of the ERG. (*A*) Response of the ERG to flicker after a number of administrations. (*B*) Under the influence of sound stimulation, the B-wave of the ERG is not remarkably changed, but the 20-per-sec. components of the ERG response are increased (as indicated by the amplitude of the peak of the 20-cps filter).

time-discriminating power of the peripheral part of the visual system is increased.

Arousal increases the negative feedback to the retina and the excitability cycle is shortened. With higher frequencies, the shortening of the excitability cycle causes a decrease in the amplitude. For example, Johnson (31), an American scientist, has shown that under the influence of reticular formation stimulation by an electric current, the electroretinographic response to single flashes of light disappeared. I believe that this disappearance is connected with the shortened period of excitation (70).

*Doty:* Have you any idea as to what might be happening to blood pressure at this time? Need this be a neuronal phenomenon?

*Sokolov:* In the studies of Jacobson and Gestring (30), perfusion experiments were done in cats, and they showed that humoral factors affecting the amplitude of the ERG were present, but the mechanism of these influences is not clear. Perhaps it is some change in potassium and calcium balance. There are results that show these influences (61). One similarity between the ERG and the visual cortex is that under the

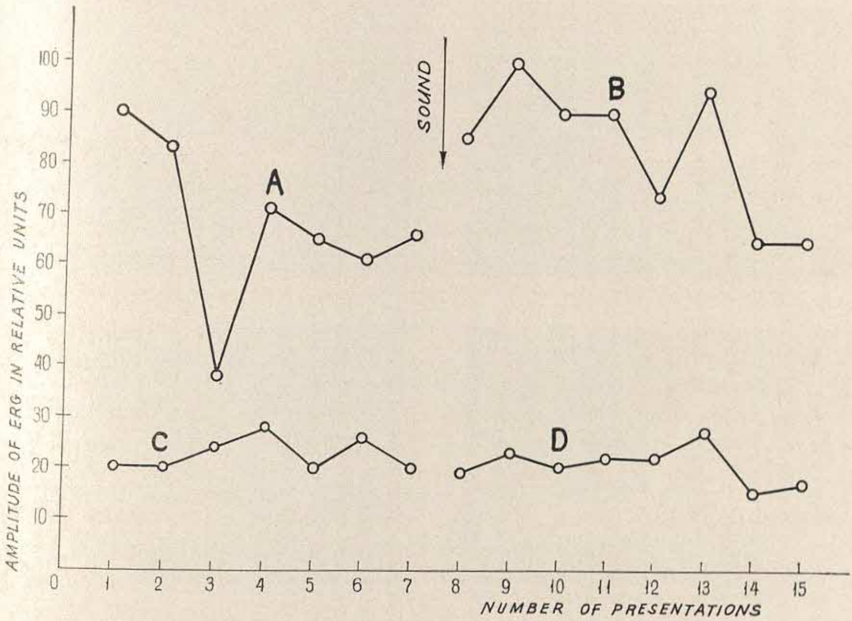

FIGURE 90. During presentation of flicker, flicker response of ERG decreases. B-wave at onset of light is not changed. After administration of sound, flicker response of the ERG increases. B-wave does not change. (*A*) Amplitude of flicker response of ERG. (*B*) Amplitude of flicker response of ERG after orienting by a sound stimulus (note increase). (*C*) Amplitude of B-wave of ERG. (*D*) Amplitude of B-wave of ERG after orienting by a sound stimulus (no change).

influence of the orienting reflex there is a shortening of the evoked responses.

To summarize the results of the first part of this report, the orienting reflex is a special functional system, which increases the discriminatory power of analyzers. I believe there are two mechanisms for this: The first is a direct stimulation through the special descending pathways to the receptors from the reticular formation and from the cortex, which can change this discriminatory power, and the second mechanism is an indirect one, a change in the blood supply of the cortex and of the peripheral part of the analyzers, which can indirectly change the excitability. The orienting reflex includes the cortical as well as the somatic mechanism of the increase in sensitivity of the visual system. These inferences can be studied in the form of a decrease in the threshold of the visual system. The experiment was conducted as

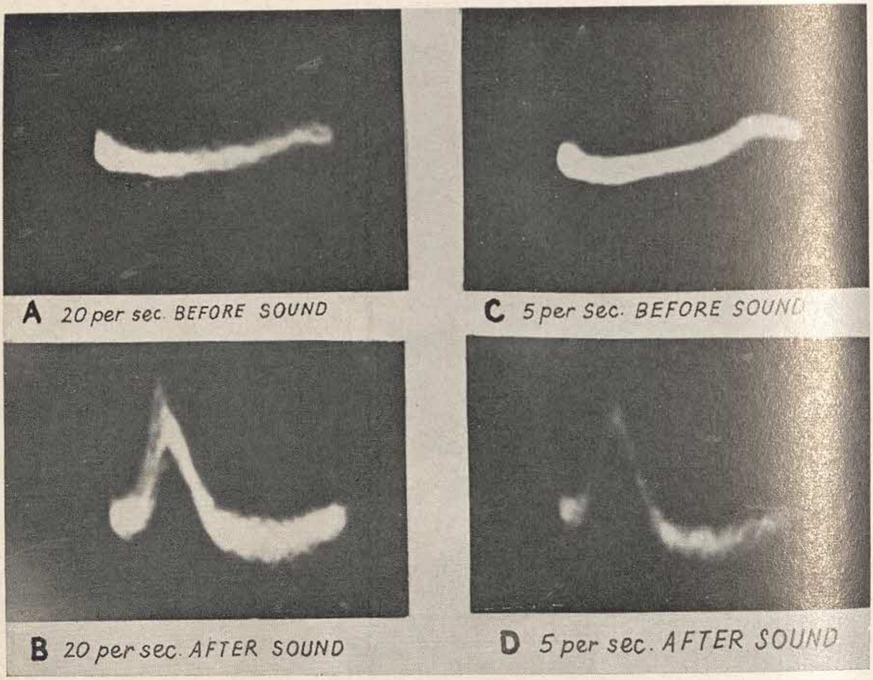

FIGURE 91. Change in shape of ERG response: (*A*) to 20-per-sec. flicker before presentation of sound; (*B*) after presentation of sound; (*C*) to 5 per sec. before sound; and (*D*) after sound. 50 superimposed sweeps of an oscilloscope. Length of sweep is 1/20th sec. for 20-per-sec. stimulation, and 1/5 sec. for 5-per-sec. stimulation; *i.e.*, each represents 1 cycle. Light-dark ratio 1 to 1.

follows: We studied the threshold of the visual system by means of test light stimulations such as are generally used in psychophysiological studies. We used a stimulus 0.8 below the threshold. When we gave this stimulation, there was no motor response and no depression of $\alpha$-rhythm. Then, after a sound stimulation, we again used this test stimulus and observed that the same light stimulation now evoked an $\alpha$-rhythm depression, and somewhat later, a motor response. This means that under the influence of arousal, the stimulation which was previously below the threshold now became above threshold. An increase in sensitivity takes place. This experiment is a form of study of sensitivity. When the sound stimulation produced no arousal and no $\alpha$-rhythm depression, this test stimulus remained ineffective after the sound presentation. This shows that the increase in discriminatory power corresponds to an increase in sensitivity in the visual system (67,71).

I believe that these data agree with some findings from the laboratories of Lindsley (38) and of Fuster (22), who have shown that under the influence of reticular formation activation, perceptual learning can be increased or become more effective.

*Leake:* Would you say that this was an example, then, of spreading excitation rather than spreading depression?

*Sokolov:* There is a depression of the $\alpha$-rhythm but, under the influence of $\alpha$-rhythm depression, the response of the visual cortex to high-frequency flicker is increased. Therefore, I believe that the depression of $\alpha$-rhythm is a sign of increased excitation.

*Keller:* How does that differ from facilitation, as we know it?

*Sokolov:* This is facilitation.

*Hinde:* Could you give some idea of how long-lasting these effects are, both the increased specificity of the orienting effect and this arousal effect?

*Sokolov:* We differentiate two forms of orienting reflex: a phasic orienting reflex and a tonic orienting reflex (66). This differentiation agrees with the differentiation of Sharpless and Jasper (62) of two forms of $\alpha$-rhythm depression—a phasic and a tonic one. Jasper has proposed that the tonic reflexes are connected with the brain stem reticular formation, and the phasic $\alpha$-rhythm depression is a result of the participation of nonspecific thalamic mechanisms activating the cortex. With repeated presentation, the period of excitation is diminished.

*Hinde:* What sort of interval do you have between presentations? When you speak about the increase in specificity of the reflex, does this last for seconds, minutes, hours, or days? And with the arousal by a sound stimulus, how many seconds or minutes does that take?

*Sokolov:* With sound stimulation, it depends on the conditions. For example, suppose the subject is in a drowsy state and we get no response. After we have made a very loud sound and the subject is aroused, there may be a long-lasting (tonic) response for about an hour. But if the arousal response is very short (phasic), there is no long-lasting shift in the direction of increased excitation. Usually the shift in excitation lasts about a minute.

Chang (15) was the first to show that there are processes of facilitation in the visual analyzer. He showed that if the visual system is stimulated by a light, there is an increase of the response to direct electrical stimulation of the geniculate body. This means that under the influence of light, facilitation in the visual pathway takes place. The influence of a sound, which I have discussed, is only an indirect influence of one sensory system on the other. I believe that this influence takes place through the participation of the reticular formation.

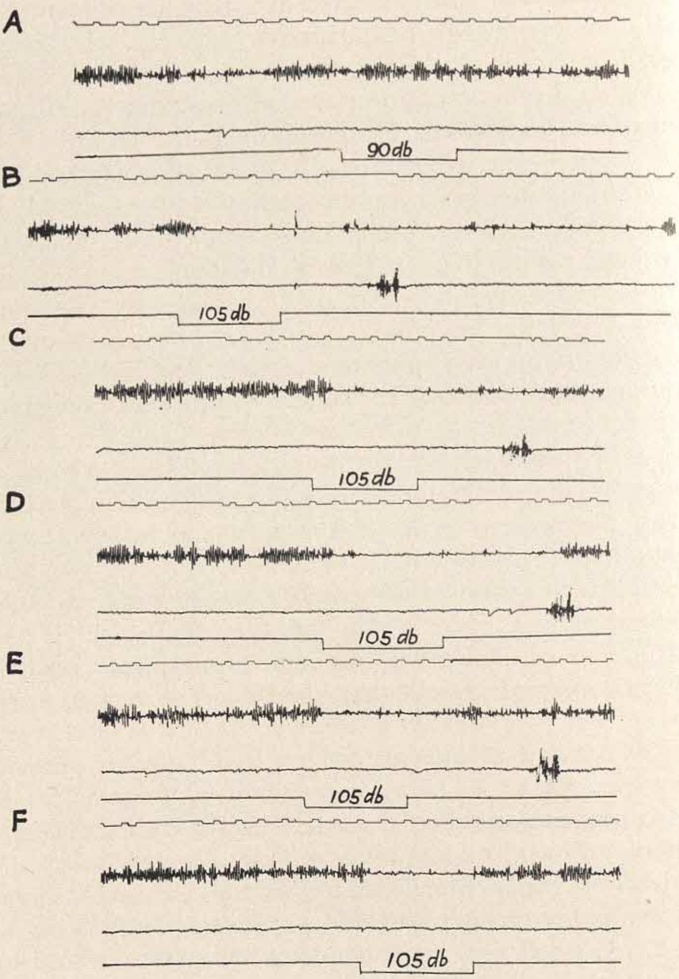

FIGURE 92. Sensitization effect under influence of acoustically produced orienting reflex in man. In (*A*) to (*F*), from top to bottom: time marker 10 per sec. broken into by signal for light; occipital EEG; EMG; signal of sound which produced orienting reflex. (*A*) After habituation of orienting reflex, sound (90 db above the threshold) produces no EEG depression or sensitization. The test light remains ineffective after administration of sound. (*B*) New intensity (105 db) produces orienting reaction EEG depression. Test light increases EEG depression and produces a motor reaction; *i.e.*, when the sound produces the orienting reflex, sensitization to light is increased. (*C*), (*D*), and (*E*) As orienting reflex habituates, sensitization effect diminishes (increasing latent period of motor reaction and decrease of EEG depression). (*F*) When reaction is completely habituated, test light produces no sensitization and does not affect EEG even after administration of sound.

*Leese:* Would you have obtained that facilitation in the secondary analyzer in a repetition of these experiments?

*Sokolov:* With repetition, this facilitation disappears. In Figure 92 we used 90 db above threshold of sound, and after repeated presentations there was habituation of responses in the brain and of motor responses to the light test stimulus. The sound was then changed to 105 db above threshold, which is very loud. The louder sound produced an $\alpha$-rhythm depression (Figure 92 *B*) and, on this background of $\alpha$-rhythm depression, the test light stimulation evoked a motor reflex and increased the $\alpha$-rhythm depression. When the response to this sound stimulation began to habituate, the latent period of the motor response to the test light stimulation was lengthened (Figure 92 *C*, *D*, and *E*), and when habituation of $\alpha$-rhythm depression to light was complete, the arousal to sound was very short. When there was a background of an $\alpha$-rhythm, there was no motor response to the test light stimulus which had previously evoked a response. This means that with the habituation of arousal, the facilitation in the sense of an increase of sensitivity is also habituated.

*Hinde:* How long does this habituation last? If tested the next day, is the animal still habituated?

*Luria:* This is not an animal, but a human being.

*Sokolov:* Two forms can be distinguished. The first is short-lasting, what Pavlov (44) called *ostroye uga shenije* (acute extinction). It is similar to the acute extinction of a conditional reflex. In chronic extinction, the mechanisms are similar to chronic habituation of the orienting reflex. After repeated presentations, the duration of habituation can be increased.

The most important feature of the orienting reflex is the habituation, but this habituation is not a generalized decrease in responsivity but a selective one. This is illustrated in Figure 93. After sixty-four acoustic presentations of 70 db, 1000 cps, no generalized or localized responses could be seen. When the frequency was changed to 500 cps, a generalized response appeared in the occipital EEG and the SGR, and those were very slight changes in the EEG of the motor region and in respiration. The application of 2000 cps evoked the same features of arousal: EEG depression, SGR, and change in respiration. With 4000 cps, the orienting reflex is even stronger than with 2000 cps; however, the greatest response is to 8000 cps. This means that although there is habituation to one frequency of the sound, reaction to the other frequency is not influenced by this habituation. The process of habituation is selective.

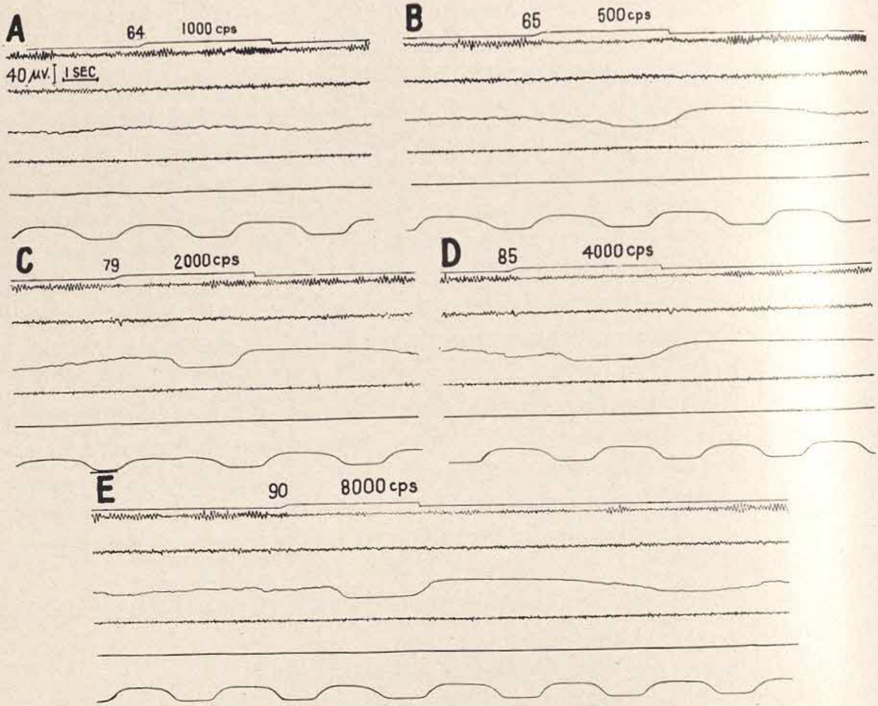

FIGURE 93. Selective habituation of different components of orienting reflex to sound (70 db). In (*A*) to (*E*), from top to bottom: signal for sound, occipital EEG, EEG of motor region, SGR, EMG, eye movements, and respiration. The first number, in each case, is the number of stimulations and the second is the frequency of tone. (*A*) Habituated to 1000 cps; no orienting reflex. (*B*) Same intensity but change to 500 cps produces generalized orienting in the form of EEG depression and SGR. (*C*) 2000 cps produces slight orienting reaction. (*D*) 4000 cps evokes prolonged EEG depression and SGR. (*E*) 8000 cps gives prolonged generalized orienting reaction (EEG depression, SGR, and change of respiration).

*Fremont-Smith:* If you were to change the frequency very slowly, would this not change the orienting reflex? If there were a very gradual change of frequency, the orienting reflex would perhaps not show itself.

*Sokolov:* That is quite another form of experiment. We can increase the frequency of the stimulation. The result is that when the stimulation increases in rate very slowly, the orienting reflex can arise. At some point, the difference is observed.

*Pribram:* Can you obtain generalization gradients? Isn't that what you are really asking? Do you get a bell-shaped generalization curve from this kind of presentation? What does it look like?

*Sokolov:* I can demonstrate this in the visual system (Figure 94), in which similar selectivity can be demonstrated.

The light stimulus was a very small light, 1° in diameter, focused on a point 40° to the nasal side of the retina. After several presentations of the light, there was a decrease in $\alpha$-rhythm depression. The SGR disappeared after two presentations of light. The local response in the visual system is more persistent than the generalized one.

But with every shift of position on the retina, even of only 10°, there was a reappearance of the generalized response in the form of an SGR. This in turn habituated on repetition. This illustrates that this habituation is very selective, in the visual system as well as in the auditory system.

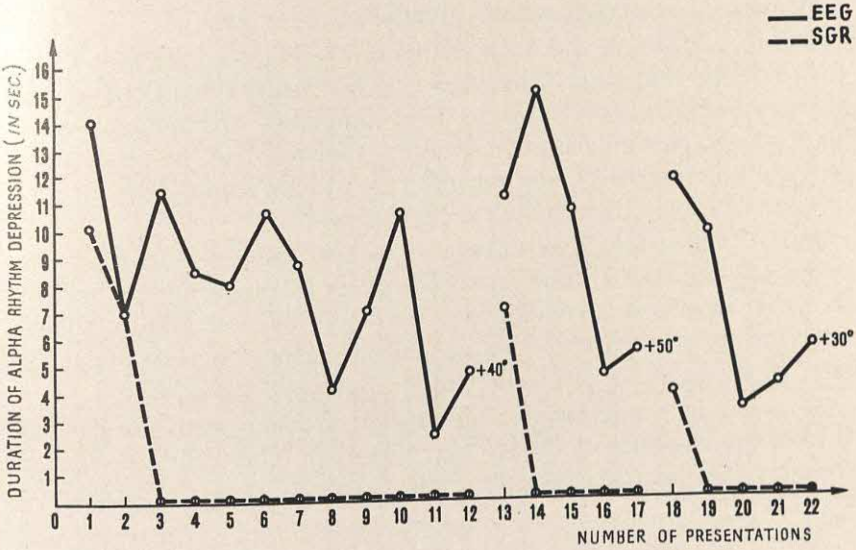

FIGURE 94. Habituation of $\alpha$-rhythm and SGR to stimulation by a light spot focused on a point on the horizontal meridian of the projection perimeter on the nasal part of the retina. After 2nd presentation, the generalized reaction is completely inhibited. The localized orienting reaction ($\alpha$-depression) is diminished only. A change of position from 40° to 50° (from the central fixation point) evokes generalized reaction (SGR and increased duration of $\alpha$-rhythm depression). Repetition of same stimulation evokes decrease in local orienting reflex and complete disappearance of generalized orienting reaction. Change to 30° produces, again, a generalized response and increase of the $\alpha$-rhythm depression. Habituation is specific to the point of retina stimulated.

*Brazier:* What is the interval between presentations of stimuli?

*Sokolov:* It is 40 seconds. We have used intervals that allowed for the $\alpha$-rhythm to reappear after the stimulation.

*Hinde:* Eikmanns (21), who was a student of Professor Birukov, worked with the prey-catching response of toads, and he found a similar extinction which was specific to the particular point on the retina stimulated.

*Sokolov:* Similar results have been obtained by Sharpless and Jasper (62), and later by Rowland (58); they have shown that the arousal response in cats is very specific and that this habituation can be very selective in relation to the frequency of the sound.

*Kelly:* You have been speaking of the sound stimulus as providing the orienting response, and the visual stimulus as being the one which was raised above subliminal levels by this facilitation. Will it work the other way around? Can the visual stimulus provide the orienting response to a subliminal sound stimulus?

*Sokolov:* I believe that such results can be obtained, because Chang (15) showed that steady illumination of the visual system can increase auditory responses evoked by electrical stimulation of the medial geniculate. Light can influence the hearing system. Also, in psychophysiology, it is known that under the influence of light stimulation, a certain increase of hearing sensitivity can be observed.

*Kelly:* Then, aren't we talking essentially about a relationship between two stimuli, not that one is by nature an orienting stimulus and the other by nature a conditioning stimulus? We are talking about a relationship between two stimuli, in which either one becomes facilitated by the other, or can facilitate the response of the other.

*Sokolov:* It is a question of the method of evaluation. We have not studied the influence of the test stimulus upon other reflexes. The test stimulus that was the subject of the particular study just mentioned was sound.

*Kelly:* But which we call the test stimulus and which we call the orienting stimulus is an artifact of our experiment, isn't it?

*Sokolov:* That is so, but it is important to understand that every stimulus has two different properties: an unspecific one which produces either a general orienting reflex or a local orienting reflex, and the specific properties which are related to the classical sensory system to which it belongs. The experiment can be performed in either direction, from sound to light or from light to sound.

*Fremont-Smith:* But in any modality, a stimulus which is near to the threshold can be made to reach the threshold by any other orienting stimulus. Is that correct?

*Sokolov:* Yes, that is correct.

*Bodian:* Isn't the main requirement that the orienting stimulus precede it?

*Sokolov:* Yes, because there is a causal connection. Therefore, it must precede the other.

*Pribram:* I would like to know, in this connection, if anyone has studied organisms below the level of the frog? Yerkes (83) reported, in 1904, that one could not get this kind of facilitation of orientation across modalities in forms lower than the frog; that this supposedly emerged at the amphibian level. Does anybody know whether this is true or how it has held up over the years?

*Hinde:* The responses of toads to equilibratory stimuli increase with light (10).

*Sokolov:* This property of selective habituation should be further explained. One might suppose that it is a drop in sensitivity but it can be demonstrated that this hypothesis is not correct for, after habituation to a strong stimulus, the presentation of a threshold stimulation can evoke the orienting reflex. Decrease in intensity is also a novelty and therefore can act as stimulation for the orienting reflex.

*Leake:* May I ask, what the relation is of the orienting reflex as you have described it to a rather gross picture that pharmacologists often talk about as the righting reflex; for example, in anesthesia, one of the first gross features observed is that the animal loses the orienting capacity and goes over on its side. In recovery from anesthesia, the ability to right itself usually comes back first. This is generally referred to as the righting reflex. Is that the same as the orienting reflex?

*Sokolov:* No, that is a different reflex. I believe that there are two different forms of the expression of the orienting reflex depending on the state of the subject at the time when the stimulus is applied. In one, the subject is in a state of excitation when the stimulus is given. The reflex then is very selective, very precise. The second form is the so-called arousal reaction, when the animal or the man is sleeping or in a drowsy state at the time of administration of the stimulus (69). The reflex is then more generalized. I believe that these experiments in animals involve this kind of activation.

*Leake:* Then, it would seem to me that the state of anesthesia or the different levels of anesthesia might be used experimentally in connection with the analysis of various aspects of the orienting reflex.

*Sokolov:* Yes. I have some data on the relationship between the

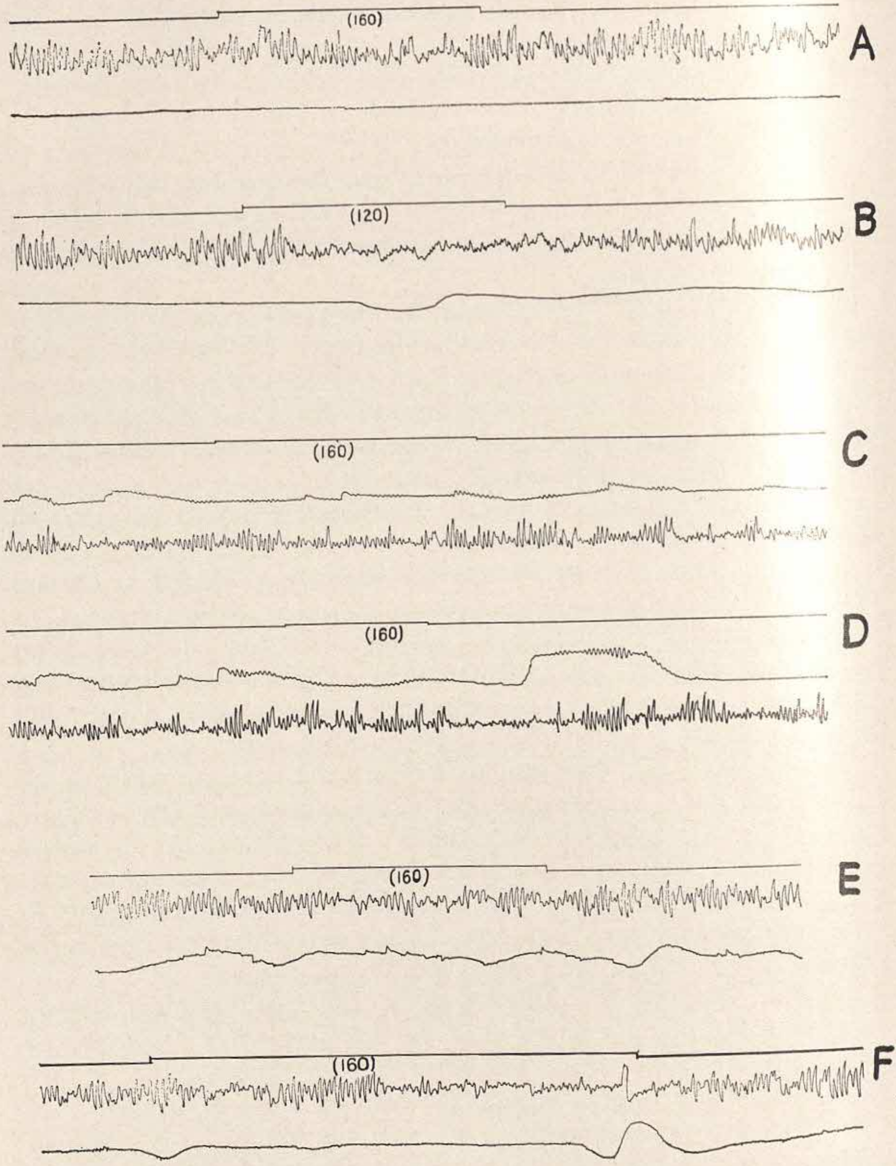

FIGURE 95. Reappearance of orienting reflex on diminishing intensity of the light stimulation. In (*A*) to (*F*), from top to bottom: signal of light in relative units, occipital EEG, and SGR. (*A*) After three sessions, complete habituation. (*B*) Diminishing light intensity from 160 to 120 relative units evokes a generalized reaction ($\alpha$-depression and SGR). (*C*) Habituation to 160 relative units of intensity with a duration of 5 sec. (*D*) Decrease in duration evokes the orienting reflex at the moment when the light is cut short. (*E*) Habituation to 160 relative units and a duration of 5 sec. (*F*) Prolongation of the same intensity evokes the orienting reflex at the moment when the duration exceeds that of the standard stimulation.

motor conditional reflex and the orienting reflex during the development of the sleep state in man. I believe such data could help to answer some of these questions.

Figure 95 demonstrates that this habituation is not a drop in sensitivity. The stimulus is a light just above threshold in intensity, and presented after 40 minutes of dark adaptation. When habituation develops, there is no response in the occipital EEG and no SGR. When the intensity of light is changed, the orienting reflex returns. There is an SGR and a marked depression of $\alpha$-rhythm.

The hypothesis is that under the influence of repeated presentations, a kind of neuronal model is elaborated in the cortex (80). What is meant by "neuronal model"? The model postulates a chain of neural cells which preserve information about the intensity, the quality, the duration, and the order of presentation of the stimuli (68,81).

We have studied this hypothesis by means of prolongation and by shortening of the duration of the stimulus. Figure 95 *B* shows that after a few presentations, each 5 seconds in length, the response disappeared; there was no SGR and no $\alpha$-rhythm depression. But when the period of stimulation was shortened to only 2 seconds, an SGR and $\alpha$-rhythm depression reappeared at the moment the stimulus was cut short (Figure 95 *D*).

According to our hypothesis, the orienting reflex is evoked when the neuronal model set up in the brain does not coincide with all the parameters of the stimulus. The orienting reflex is produced not only by the stimulation itself, but by impulses arising as a result of noncoincidence between a certain cortical pattern (the model) and the applied stimulation.

*Fremont-Smith:* Could you say that the central nervous system has an expectation as shown by the model?

*Sokolov:* I think expectation is too broad a term, too diffuse a concept. I believe that a certain system of neural cells preserves the properties of the applied stimulation.

*Fremont-Smith:* A kind of memory?

*Sokolov:* Yes, that's right.

*Fremont-Smith:* And then a new stimulus comes in, since you have a new orienting reflex?

*Sokolov:* But the factor of novelty should be explained. What is meant by "novelty"? Novelty is the noncoincidence between the stimulation and the elaborated neuronal model.

In Figure 95 *F*, the period of stimulation was made longer, and as a consequence the $\alpha$-rhythm was depressed at the point where the duration of the usually applied stimulation ordinarily ended. I believe that these experiments support the hypothesis that a certain neuronal model is formed, and that the orienting reflex is a result, not of the stimulation itself, but of impulses caused by the difference between the model and the stimulation.

The nervous system apparently forms a certain program of stimulation. This program is compared with the real stimulation. If the stimuli do not coincide in all parameters, an orienting reflex is evoked at each point of disagreement. This effect serves to increase discriminatory power for the obtaining of new information about the unusual properties of the stimulus.

*Fremont-Smith:* Would you say that any change in the Gestalt would give an orienting reflex?

*Sokolov:* I am not satisfied with that concept, because what does change in Gestalt mean? There must be something specific in the brain which is compared with the stimulus. It is the disagreement between this model and the stimulus which evokes the orienting reflex.

*Fremont-Smith:* Yes, but I am trying to say that any disagreement in the total picture, any change in any property, will be sufficient to evoke an orienting reflex.

*Brazier:* Professor Sokolov, would you be more satisfied if this were put into the language of information theory rather than Gestalt? When bits of information come through to the brain, there will be an orienting reflex.

*Sokolov:* Yes, that's right, although I have no actual measurement of the amount of information. It should be measured.

*Brazier:* Yes, but this would bring in the concept of probability of the nervous system's having experienced this before. The less probable the stimulus, the more information will come through.

*Sokolov:* That is right.

*Pribram:* First, a set must be established out of which events are to be selected, "setting the stage," as it were. The second step does not occur until after the first. In a sense, this goes beyond information theory, because it sets the limits on the number of alternatives out of which selection can then be made. Only then does information measurement begin.

*Sokolov:* But information theory can be used in all cases where the stimuli can be characterized by their probability of occurrence. When a stimulus is repeated, the probability of its occurrence is increased, and therefore the amount of information it conveys is decreased.

*Purpura:* Is this neuronal model elaborated in the "second signal system"? And have you studied it?

*Sokolov:* Yes, we have studied this phenomenon in the second signal system and have found that after habituation of response to a word, another word of similar semantic meaning does not evoke an orienting reflex, whereas a word of a different meaning does. A very complicated system can be introduced in this process.

*Fremont-Smith:* I would like to go back for one minute to the word I used, "expectation," because it seems to me that it somehow fits this broader concept of the repeated stimulus. Probability is another way of saying expectation. When the unexpected, unanticipated, or new, takes place in any dimension of the pattern, there is the orienting reflex. Is that all right?

*Sokolov:* That is all right, but I should emphasize once more that the concept of expectation is not a measurable one. I use the term "model" because I want to measure its properties.

*Pribram:* The word, "expectation," has a precise meaning in mathematics. It means a summation, an averaging. We are talking here about something else, and that is perhaps why the word, "expectation," should not be used in this particular instance. Here we are concerned with an information measurement model, which is different from an expectational one.

*Hinde:* Professor Sokolov, when you say that if the stimulus does not coincide with this neuronal model an orienting reflex results, shouldn't you also say that a conditioned response results when the stimulation coincides with the neuronal model?

*Sokolov:* That is right.

*Magoun:* Would you like to relate this to the problem of habituation? Is it a stimulus to which the subject is not habituated that produces the orienting reflex? Earlier, you pointed out that with repetition, a stimulus fails ultimately to evoke an orienting response, *i.e.*, to induce an alpha blockade and an SGR. These were your two indices, were they not?

*Sokolov:* That is right.

*Magoun:* Then, when you introduced a stimulus to which the subject had not been habituated, the orienting reflex reappeared. Is it this quality of novelty, in the sense that there had not previously been an habituation to the situation, that leads to the orienting reflex? Is this expression acceptable to you?

*Sokolov:* There are three different descriptive terms for this process. *Habituation* is a descriptive term; *extinction* is a term derived from the theory of conditional reflexes and connects this process with the extinction of a negative conditional reflex. The third term describes the physiological process which underlies this process, namely *inhibition.*

*Leese:* There was another term, Professor Sokolov, that I believe you used earlier in your discussion, and I would like to ask about it since we're talking about terms. I remember you used the word, "adaptation." By adaptation, do you mean the loss of the orienting reflex, or were you using it in the same sense as a conditioned response?

*Sokolov:* I used the term "adaptation" only in relation to the adaptive reflex. This is a specific reflex which is related to the intensity and quality of the stimulus. For example, the pupillary reflex: the stronger the light, the more restricted the pupil, and vice versa. The orienting reflex does not depend on the quality of the stimulation. Therefore, I discriminate between the orienting reflex and the adaptive reflex. But, in general, in biological terms, adaptation is often used for all processes of adjustment of the organism to its environment.

The next problem is the explanation of the function of this neuronal model, which is to filter the signals in the nervous system. This means that a selective prevention of transmission of impulses from certain kinds of stimulation must take place. We can measure the property of this biological filter by changing stimuli and by measuring reaction.

*Leake:* Does the concept that you have of filtering-out involve the process of inhibition?

*Sokolov:* That is right, but I want first to describe, quite formally, the properties of a biological filter, and then go on to explain the structural scheme of the orienting reflex. In Figure 96, we measured the duration of the $\alpha$-rhythm depression after habituation of the response to 1000 cps. After habituation to the sound at 1000 cps, the response to other frequencies is then greater in proportion to the difference between 1000 cps and the frequency used as the new stimulus.

It is important to discuss the relationship between the neuronal model and the Pavlovian concept of a "dynamic stereotype." By a "dynamic stereotype," is meant a special pattern of responses that is reproduced in accordance with previous experience. For example, light, sound, and tactile stimulation produce a different magnitude of reaction, but if, after each has been given, we present only one of these stimuli, we find that it alone reproduces the characteristic responses of the other stimuli.

This is what was called the dynamic stereotype, for there is a stereotyped reproduction of the reaction. "Neuronal model" is a term which is used for the understanding of the *non*stereotyped orienting reflex for, in the orienting reflex, reaction is not stereotypically reproduced but is

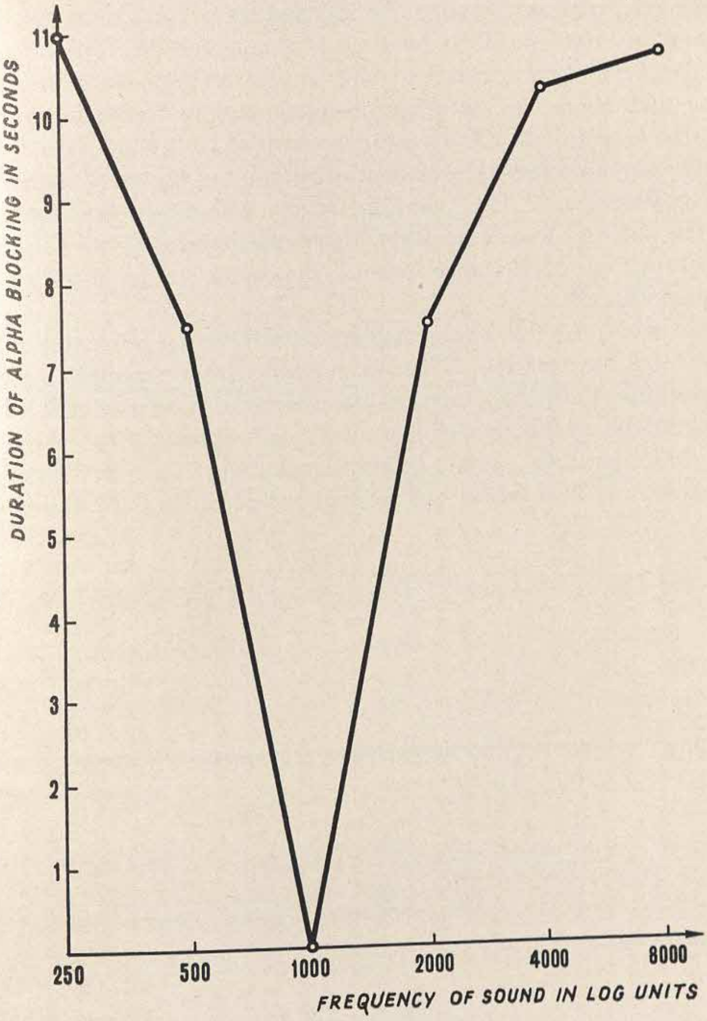

FIGURE 96. Characteristics of the filter in the neuronal model. It is evident that there is a selective filtering of the impulses to the habituated frequency and that the responses to other frequencies are greater, the greater the difference between them and that of the habituated sound. This is a negative filter, and it prevents the transmission of impulses from the applied stimulus to the neurons responsible for organizing the orienting reaction.

evoked only when there is a change of stimulus. I believe, however, that the neuronal mechanisms of these phenomena are the same, and a comparison between the orienting and the conditional reflex supports this view.

The next problem concerns the mechanism of this neuronal model. The most interesting results have been obtained in the drowsy state in man. In these experiments we used sounds, and on repetition in the waking state there was complete disappearance of the orienting reflex. When the background activity in man changed to that of a drowsy state with delta and theta waves instead of alpha, we observed a very interesting phenomenon. The orienting reflex, which had previously been inhibited during the waking state, reappeared and was not inhibited in spite of dozens of presentations of the same sound stimulus while drowsiness lasted.

Figure 97 shows that in this subject, after the first presentation, there was an orienting reaction. This was a generalized response. After four presentations, no further response was observed. Then, after this habituation, a change in the state of the subject was observed and theta waves appeared in the EEG. As can be seen from Figure 98, when there was a background of theta waves (in spite of the previous habituation of the

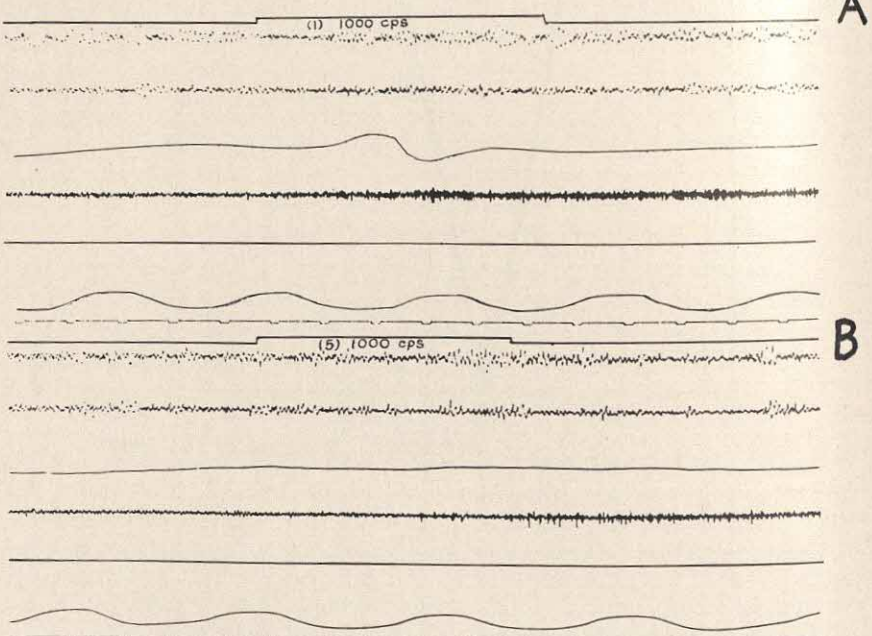

FIGURE 97. Habituation to sound (150 db, 1000 cps). In both (*A*) and (*B*), from top to bottom: the signal, occipital EEG, EEG of motor region, SGR, EMG, eye movements, respiration, and time marker in seconds. After four presentations of this sound, all signs of the orienting reflex disappear.

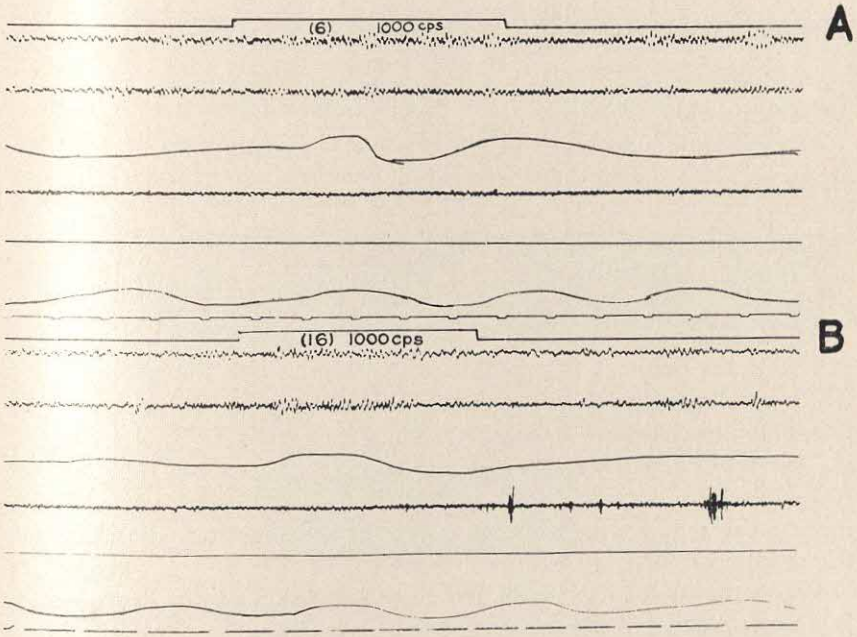

FIGURE 98. Continuation of Figure 97. (*A*) When an inhibitory state of cortex develops (note theta waves in EEG), there is a paradoxical recovery of orienting reflex (EEG change and SGR), indicating increased stimulation and decreased inhibitory control of impulse transmission. (*B*) Although in the awake state five presentations produced complete inhibition of orienting reflex in this subject, in the drowsy state there is no decrease even on the 16th presentation.

orienting reflex in the fully waking state), the same stimulation produced return of $\alpha$-rhythm, and also recovery of the SGR. This activation of a vegetative function indicates that, under the development of an inhibitory state of the cortex, some inhibitory control of this vegetative function is lost.

*Doty:* Are the latencies of the SGR's the same under these conditions?

*Sokolov:* In general, the latency is the same, in spite of the number of presentations. After four presentations when the subject was awake and in a state of excitation, the orienting reflex was inhibited. When he was drowsy, it was not inhibited; neither the SGR nor the EEG change habituated.

This suggests that habituation is the elaboration of an inhibitory conditional reflex regulating the transmission of impulses to the reticular formation. This hypothesis is supported by some data obtained in France by Benoit (9), who stimulated the reticular formation electrically and observed no habituation of arousal. Therefore, I believe that the block of impulses takes place somewhere between the collaterals from the specific pathway and the reticular formation.

We can explain it as follows: the beginning of stimulation in every case is one stimulus, and its prolongation acts as a second one. According to this hypothesis, the prolongation of stimulation produces an unconditioned inhibitory process which can develop during a sufficiently long presentation of each stimulus. We assume that this process arises between the collaterals and the reticular formation, probably by hyperpolarization of synaptic connections.

After repeated presentation of the same stimulation, the beginning of this stimulus becomes the conditioning stimulus for the prolongation which produces the inhibitory state. This conditioned inhibition of inflow into the reticular formation results in signals being transmitted via the specific pathways before the stimulation reaches the reticular formation and the nonspecific system; in this way, the specific transmission can regulate the transmission to the reticular formation through the mechanism of a conditional reflex.

When the cortex itself is in a state of inhibition (as in drowsiness), this active control of the subcortical level is excluded or diminished, and therefore impulses can reach the reticular formation in this state.

*Keller:* Is there any special reason to think that these impulses would have to pass by way of the reticular formation? Couldn't they go through the thalamus as such? If you had stimulated the long ascending tracts going directly into the thalamus, wouldn't you do the same thing?

*Sokolov:* I don't know because I have no direct experiment, but I believe that every long stimulation produces at its onset a state of excitation which later disappears and is replaced by an inhibition. For example, in a dog with a cortical lesion that prevents normal habituation, the orienting reflex can disappear if the stimulation is prolonged.

I believe that disinhibition of vascular responses in the state of sleep is very important. It is well known that sometimes, in the drowsy state, cardiac reflexes are increased. We have obtained similar results, not only with the orienting reflex, but also with this specific reflex, namely, the change of vascular responses with cold and with warmth. After very many presentations of cold in the waking state, habituation to this specific stimulation can occur (Figure 99). But during sleep, the orienting reflex and the specific reflex are both increased, and at the same time there is a marked change of respiration and a reappearance of the SGR. We have never observed such a change of respiration in the waking state. This marked response is a disinhibition.

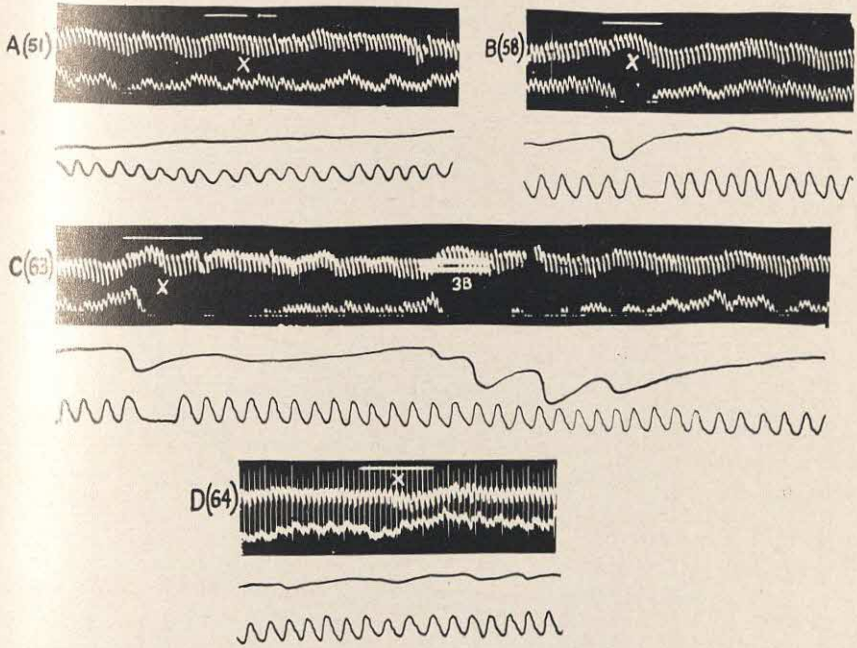

FIGURE 99. Orienting and adaptive reflexes in sleep. In (*A*) to (*D*), from top to bottom: vascular reaction in the head, vascular reaction in the hand, SGR, and respiration. Application of cold is indicated by (x) and sound is indicated in (*C*) by 3B. (*A*) At 51st application of cold (0°) to the skin, when awake, no orienting and no adaptive reflexes are seen. (*B*) At 58th, with onset of sleep, the orienting reflex reappears (vasodilation in head, vasoconstriction in finger, SGR, and arrest of respiration). (*C*) At 63rd, recovery of the orienting reflex in sleep. A loud sound produces a marked orienting reflex and a shift of excitation, which is evidenced by the increased SGR. (*D*) At 64th, after awaking, the orienting and adaptive reflexes are once again automatically inhibited.

The cold produced no effect after arousal. This shows that in the inhibitory state of the cortex, some active inhibitory control is lost. It is possible to differentiate two mechanisms: one, a certain level of excitatory state in the cortex, and the other an inhibitory process. These are coordinated so that one functional system can be inhibited and another activated. This changeable state of the cortex can influence the vegetative system and the different reflexes. Therefore, in our hypothesis of habituation, we introduced a neuronal model with active control from the cortex over the vegetative system and the reticular formation. The character of this control depends on the state of the cortex.

Figure 100 is a schematic concept of the orienting reflex. It includes

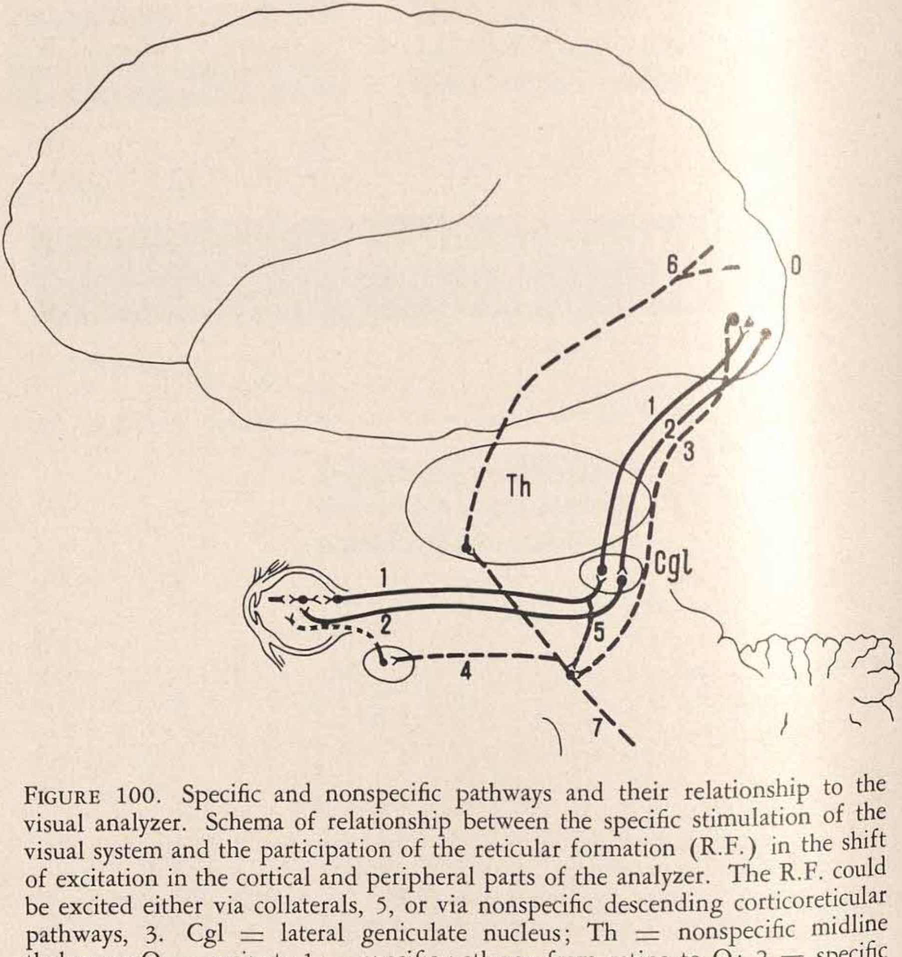

FIGURE 100. Specific and nonspecific pathways and their relationship to the visual analyzer. Schema of relationship between the specific stimulation of the visual system and the participation of the reticular formation (R.F.) in the shift of excitation in the cortical and peripheral parts of the analyzer. The R.F. could be excited either via collaterals, 5, or via nonspecific descending corticoreticular pathways, 3. Cgl = lateral geniculate nucleus; Th = nonspecific midline thalamus; O = occiput; 1 = specific pathway from retina to O; 2 = specific descending pathway from O through Cgl to retina; 3 = nonspecific descending pathway from cortex to R.F.; 4 = pathway from R.F. to sympathetic ganglion and retina; 5 = collateral from the specific pathway leading into R.F.; 6 = nonspecific ascending pathway from Th to O; and 7 = ascending and descending pathways in R.F.

the specific pathway to the occipital regions, with a specific feedback to the visual receptors. This feedback has been demonstrated in the work of Poliakov (46) and of Shkolkin-Iarros (64) who studied the return pathway from the cortex to the geniculate body and to the retina. The collaterals to the reticular formation are also shown. Broken lines indicate nonspecific pathways including the connection between the brain stem reticular formation and the thalamic region, as well as the cortico-reticular pathways for control of the reticular formation, and a pathway from the reticular formation through the sympathetic ganglia, a connection which regulates the level of excitation of the retina.

During habituation, specific impulses reach the cortex, and from the cortex there is a kind of regulation of the transmission of impulses from the collaterals into the reticular formation, and, then, if arousal takes place in the reticular formation, the receptors as well as the cortex can be activated.

This schema (Figure 100) for the orienting reflex thus includes the neuronal model in the cortex, the feedback control of transmission from the specific tracts to the reticular formation, and activation from the reticular formation upon the receptors and the cortex. It has been drawn for the visual system but different pathways serving the SGR and respiration also exist. They are not shown in this diagram.

*Pribram:* One thing is omitted in this diagram, the functions of the limbic formations in this whole process. These were discussed here at the Second Conference on The Central Nervous System and Behavior.

*Sokolov:* I have no experimental results. I know the results of Lissák and Grastyán (39), which are also known here. I believe that inhibitory influences can be produced from different parts of the brain, not only from the limbic system.

Figure 101 is a quite schematic representation of a model system in the cortex with an amplifying system in the reticular formation. Stimulation can reach the modeling system by the specific routes (1, in Figure 101), or the amplifier through a collateral (2, in Figure 101). The cortex can exert an inhibitory control that prevents these impulses from reaching the amplifying system (3, in Figure 101). The influence from the reticular formation upon the cortex increases the discriminatory power of the modeling system (4, in Figure 101). When there is no coincidence between the stimulation and the model, impulses pass from the cortex to the reticular formation (5, in Figure 101).

The process of habituation of the orienting reflex can be regarded as a blocking of the impulses to the reticular formation, mediated by specific control. The speed of conduction of impulses in a specific system is greater than in a nonspecific one, and probably it is possible to block these impulses before they reach the reticular formation.

On repeated presentation, two processes take place: the elaboration of a neuronal model and the elaboration of the conditional inhibitory reflex, which makes it possible to block these impulses. If there is a change in the stimulus, the noncoincidence between it and the neuronal

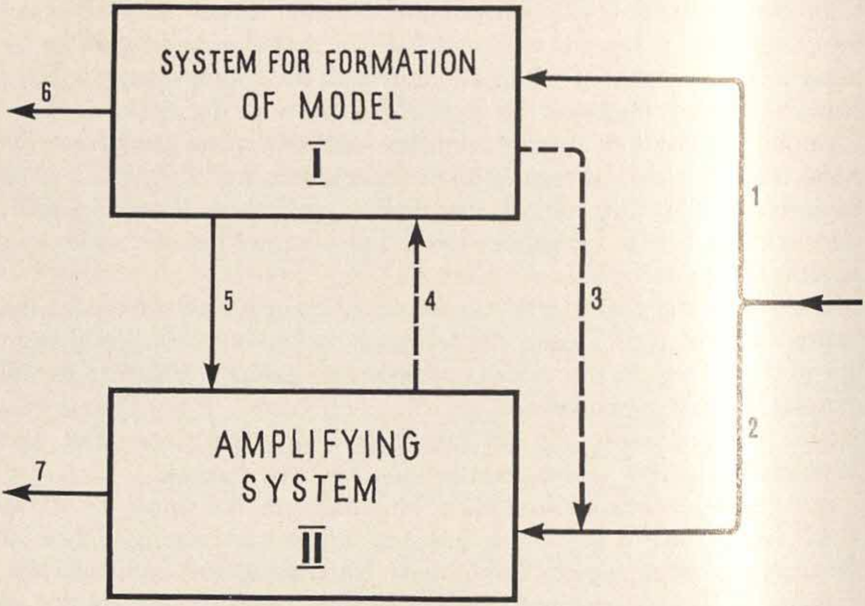

FIGURE 101. Schema for the orienting reflex. I. Modeling system. II. Amplifying system. 1 = specific pathway from sense organs to cortical level of modeling system; 2 = collateral to reticular formation (represented here as an amplifying device) ; 3 = negative feedback from modeling system to synaptic connection between collaterals from specific pathway and R.F.; 4 = ascending activating influences from the amplifier (R.F.) upon modeling system (cortex) ; 5 = pathway from modeling system to amplifying system (this is the pathway through which the impulses signifying concordance are transmitted from the modeling system to the amplifying system) ; 6 = to the specific responses caused by coincidence between the external stimulation and the neuronal model elaborated in the cortex; and 7 = to the vegetative and somatic components arising from the stimulation of the amplifying system (R.F.).

model produces activating impulses from the cortex to the reticular formation. The conditioned inhibition is weakened by the change in stimulus. On repeated presentation of this new kind of stimulation, a new model is formed.

*Doty:* How do you include temporal patterning? The impact, after all, is not one of only the initial event, but of neurons with different firing frequencies and firing patterns. I can see where you might imagine the specificity coming from the cortical threshold back to the reticular system on a point-to-point anatomical basis, but how, in the temporal aspect, is it going to select one frequency of input from another frequency of input over thousands of neurons? In other words, I can see this anatomically, but not physiologically, in terms of time.

*Sokolov:* There are different theories about the mechanism of memory. One theory regards the neuron as a mechanism which can be either in an excitatory state or an inhibitory state, one binary digit of information to a neuron.

Another theory is that in the neuron, the information is coded in the ribonucleic acid. Morrell (41), for example, has studied different parts of the cortex in a learning situation and has made comparison with the chemical changes in cortical cells. He has postulated a mechanism for memory at a molecular level. According to his concept, different aspects of the stimulation would be coded at the molecular level. It is not easy to explain.

I might mention some additional experiments that are the work of Anokhin (3). He showed that if the tongue of a dog is touched by a certain chemical substance, the first impulses evoked are tactile; then impulses conveying the temperature of the substance are evoked; and then, with the longest latent period, impulses specific to chemical stimulation are evoked. The first train of impulses can be conditioned to the next train of impulses. Anokhin regards this unconditioned reflex as a very complex structure, in which some mechanisms of conditioning take place. For he has found that, in certain circumstances, the response to chemical properties of stimulation can be reproduced with a latent period which is shorter than the time taken by impulses to reach the cortex. With repeated presentations, the initial tactile impulses may become the signal for the chemical impulses that follow.

*Leake:* Tunturi, of the University of Oregon, has done some significant work on the auditory cortex in the dog. He has shown almost specificity of discrete areas of cortex to specific sound frequencies; the response of the cells in a given area occurs only to a specific sound frequency (74,75).

*Sokolov:* Those experiments are supported by the work of Galambos (23), who showed that, depending on the intensity of sound stimulation, the number of cells which are included in the response is larger the greater the intensity. If the intensity is near to the threshold, the cells respond to one frequency only.

This assumption that one neuron responds only to one frequency would mean that it can discriminate intensity only. It is my belief that this finding is very important for the elaboration of hypotheses about discrimination. The coding of intensity by neuronal impulses is well known. The number of impulses is a log function of the intensity of stimulation. Therefore, if one neuron does indeed respond only to one frequency, the problem of perception would be reduced to the perception of intensities of different single properties.

*Leake:* In connection with the specificity of certain cells to a frequency, I think that the cells are serially arranged. Is that right?

*Sokolov:* It is very difficult to explain all the details. I believe that the work of Jung (33,34) showed that so-called "A" neurons of the occipital cortex, which are nonresponsive to light, can, under the influence of stimulation of the reticular formation, become responsive. Therefore, the number of neural cells involved in a reaction is not necessarily constant.

*Doty:* You're getting back to the reticular formation now, the control of the cortical input.

*Sokolov:* Yes, that's right, and it is very important. In the work of Jung (33,34), it was shown that the discriminatory power of one neuron (type B or E) is increased under the influence of stimulation of the reticular formation, for it can then discharge at the rates of higher frequencies of flickering light than before. This must mean that the amount of information received by one neural cell is also increased when the reticular formation is stimulated. There is a connection between the nonspecific influence of the reticular formation and the specific properties of the neuron's reaction to impulses initiated by light.

*Leake:* There is another point that I think is of interest here in regard to the inhibitory feedback. This is in connection with a principle of reciprocal inhibition. Retzlaff (54,55) recently reported in *Science* that if a stimulus is put into one of the paired Mauthner's cells in the goldfish through the eighth nerve, one cell will be stained in a certain way, whereas the corresponding cell will be stained in a different way. These can be reciprocally shown if the stimulus is put in the other way; in other words, one of the Mauthner's cells is activated, whereas the other is inhibited, and there is known to be an anatomical pathway between the two cells; so that the anatomical feature of the inhibitory feedback is clear in those two paired cells (54,55).

*Sokolov:* I agree with you, that the role of negative feedback is likely to be a universal form of regulation of the neural cells. I recall Kuffler's work (37) on the responses of rapidly adapting stretch receptors that are influenced by a negative feedback which hyperpolarizes the level of generating potential. Then, there is Dr. Purpura's proposal that the negative feedbacks in the cortex may regulate dendritic activity. We know that the motor neuron in the spinal cord is regulated by feedback to inhibitory Renshaw cells. This may be a universal property of the nervous system found at different levels.

*Leake:* The study of reciprocal inhibition on the paired Mauthner cells in the goldfish suggests that all neuronal models would be paired, as it were, with the reciprocal sets of muscles that are involved. But I ask, is there any evidence of this in any other species?

*Sokolov:* I don't know.

*Livingston:* I may have missed some quite central aspects of your discussion, Dr. Sokolov. I would like to ask for some elaboration of the evidence which inclines you, as I understand it, to place the filter in the cortex.

*Sokolov:* I believe that there are now two pieces of evidence for the presence of this filter in the cortex. The first is the existence of filters for functions that are solely cortical, for example, the complex discrimination of words. The second piece of evidence is that the development of slow waves in the cortex, the inhibitory link is diminished. This is also some evidence for control by the cortex.

The studies of Sharpless and Jasper (62) have shown, however, that this is a very complicated subject, because the discrimination of single frequencies can take place at the thalamic level too. But, after the removal of the temporal lobe, they found no habituation to pattern. For example, they had used rising frequencies and decreasing frequencies, and selective habituation to the direction of change in frequency was lost after the destruction of the temporal lobe. Similar results have been found by Rowland (58). Therefore, I believe it is possible that models can form at different levels of the brain, but I don't know how the recovery of the orienting reflex in the presence of theta waves can be accounted for except as essentially a cortical phenomenon.

*Livingston:* In drowsiness, although theta waves are observed at the cortical level and it can properly be assumed that cortical function is correspondingly interfered with, can it not be that other parts of the nervous system are also affected? If this is the case, you would not be compelled to place the filter in the cortical region on this evidence alone.

*Sokolov:* That is right. It may be that in the process of rehabituation there is a very complex relationship between the limbic system and the cortex. But, in general, the impression is that the role of the cortex is very important in this process.

*Pribram:* Perhaps, the limbic system could control the time constants of the process diagrammed by Professor Sokolov. These processes must be dependent on very precisely timed circuits, and if their time constants are changed, the whole process might well be disturbed. It could be that the limbic formations control the time constant of the system, as was discussed here at the Second Conference on The Central Nervous System, whereas the filtering process *per se* actually takes place isocortically.

*Brazier:* Professor Sokolov, as I understand your schema, and from what you have said of the effect when your subject went to sleep, you were thinking in terms of a block of the collateral inflow into the reticular formation. Did I understand you correctly?

*Sokolov:* That's right, but this is based on indirect evidence, because I have no experience with electrical stimulation of the reticular formation and the study of inhibition of this response. But I know from the work of others that direct stimulation of the reticular formation in this case does not result in habituation (9,60).

*Brazier:* I was interested, because there is some evidence that the collateral inflow into the reticular formation is where the block with ether takes place. I wondered if you had tried your experiment on a subject in very light ether anesthesia, to see whether or not you got the same effect as in drowsiness.

*Sokolov:* It is true that selective blocking can also be present in the sleeping state. For example, the work of Sharpless and Jasper (62) was conducted in the sleeping cat, and they showed that arousal of the cat could also be selective.

*Luria:* We are now planning together a series of experiments on human beings with tumors in different regions of the brain. We started this only a few months ago, so I can't report results, but our first impression is that there are pathological cases in whom there is no extinguishing of the orienting reflex, and those are cases not of cortical disturbance but of subcortical disturbance.

*Doty:* The question is whether the evidence points exactly to a cortical locus, but I think we should recall in this connection Jouvet's (32) experiments, which show that one does not even get electrophysiologically defined sleep without the presence of neocortex, nor does one get habituation. This would point to the necessity of neocortex in these phenomena.

*Lowell:* I think another point that would bear on Dr. Livingston's question is Professor Sokolov's finding that habituation can be avoided by instructing the subject to count the number of sounds he hears, or press a button. This will prolong the initial orienting response for, I believe, 100 to 150 trials. Isn't that right, Professor Sokolov? Would you interpret that as further evidence for the cortical location of your neuronal model or your filters?

*Sokolov:* Yes, but this is a subject which we should discuss further, because the counting of signals is a kind of conditional reflex, and therefore it is a problem of the influence of conditioning upon the orienting reflex. I believe it to be a special case.

*Bridger:* Professor Sokolov mentioned to me before that in the Soviet

Union, similar studies have been made with habituation of newborn babies. He was studying 2-hour old babies and got the same kind of habituation. They were able to habituate a baby's startle response to sound in one spatial area and when they moved the source to another they got the startle again. The baby was sucking at the time and they used this stimulus to inhibit the sucking. They habituated out the external inhibition and then switched back.

*Leese:* We have been observing some orienting reflexes on medical students in order to measure the latency of increased heart rate to anticipated stress. Following the signal to squeeze a dynamometer, these subjects orient in less than the time of one or two heart beats. It is quite interesting also that if exercise is in progress, and a signal is given to anticipate rest soon to come, "inhibitory" orientation is observed. The subject usually decreases the heart rate in the time of a couple of heart beats, even though the metabolic demands of exercise are still in progress.

*Sokolov:* Some aspects of the orienting reflex could be discussed further in connection with the problem of the conditional reflex, because so far we have considered only the case of the orienting reflex in response to stimulation. But one can also study the orienting reflex during the elaboration of a simple or a complex conditional reflex.

I can summarize in a few words the role of the neuronal model in the context of the orienting reflex. First, the neuronal model is a multidimensional filter of stimulation. The degree of habituation depends on the probability of the applied stimulus. This means that if several different stimulations are used, the magnitude of the response is in inverse proportion to the probability of the applied stimulus. These two propositions are important for the understanding of the application of the theory of the neuronal model to conditional reflexes.

When attempting to use the concept of this neuronal model for the understanding of conditional reflexes, it should be recognized that either the conditioning stimulus or the reinforcement (which is used when they are combined) can evoke both the orienting reflex and the specific reflex; the elaboration of the conditional reflex is a complex interaction between orienting and specific reflexes evoked by conditioned and unconditioned stimuli (67,76).

In our experiments for study of the relationship between specific and orienting reflexes during the elaboration of the conditional reflex, we use a previous habituation of the orienting responses to conditioned and to unconditioned stimuli. Figure 102 illustrates the elaboration of a defensive conditional reflex to a combination of sound and electric

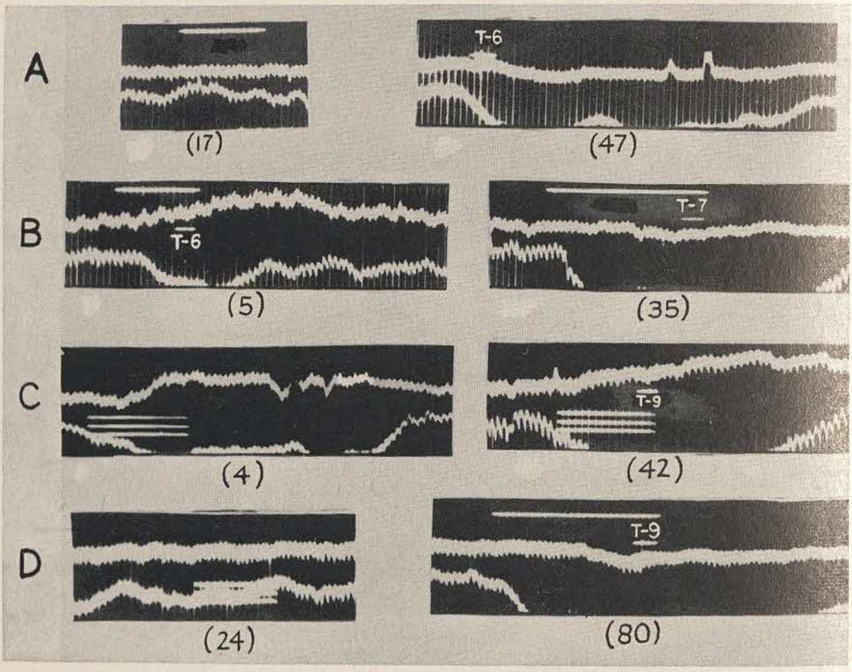

FIGURE 102. Relationship between orienting and conditional reflex. Sound, indicated by long horizontal lines, strength of electric shock indicated in arbitrary units (T-6, T-7, T-9). In (*A*) to (*D*): upper traces, vascular reaction in the head; lower traces, in the finger. (*A*) After 17th sound and 47th shock, no orienting reflex. Sound alone has no effect (left). Shock alone (T-6, right) produces defensive reflex (vasoconstriction in both head and finger). (*B*) Combination of sound with shock in elaboration of conditional reflex at first evokes orienting reflex to both the sound and the as yet unconditioned shock (left, 5th combination). Only after the 35th combination was defensive reflex elaborated (right) *i.e.*, vasoconstriction in the head on sound preceding application of shock. (*C*) A different sound evokes recovery of orienting reflexes to both the new sound and to the previous conditioning stimulus (left). When one sound is reinforced with shock and the other not, the orienting reflex is very marked and persistent. Even after the 42nd presentation and increase of the shock to 9 units, the orienting reflex is still present (right). (*D*) During elaboration of conditional reflexes, the differential stimulus becomes ineffective, and the conditioning stimulus begins to evoke the defensive reflex (24th and 80th).

shock. The upper trace is the vascular response of the head. Below is the vascular response of the hand. There is habituation of the orienting reflex after seventeen presentations of a sound as evidenced by lack of response in the vascular systems. At the forty-seventh presentation of electric shock alone, a defensive reflex develops which is expressed in the vasoconstriction of the vessels of the head and vasoconstriction of the vessels of the finger. When the sound is combined with the shock, the first effect is a return of the orienting reflex (Figure 102 *B*, left). The combination of sound and shock at first evokes the orienting reflex (vasodilation in the head, vasoconstriction in the finger). Only after thirty-five presentations does a conditional defensive reflex become elaborated. The sound then produces the vasoconstrictive reaction in the head (indicative of the defensive reflex) before the application of the electric shock (Figure 102 *B*, right).

With the introduction of an additional, new sound, which has to be differentiated from the previous one, there is a marked increase in the orienting reaction. This new sound is not reinforced by a shock. There is now also an orienting reflex to the old stimulation, the previous sound, which before had evoked only the defensive reflex (Figure 102 *C*, left). This means that the orienting reflex is important at the beginning of the elaboration of a conditional reflex and again becomes necessary in starting the elaboration of a differential conditional reflex. Only after seventy-nine presentations of the reinforced stimulation can we again observe the conditional defensive reflex as evidenced by vasoconstriction developing in the head before the arrival of the shock (Figure 102 *D*, right). After twenty-three presentations and nonreinforced stimulus, there is an absence of the orienting reflex as well as of the defensive reflex (Figure 102 *D*, left).

I believe that this scheme is important for understanding first, that the orienting reflex is a special, separate system from that of the conditional reflex; and second, that the orienting reflex is nevertheless closely related to the conditional reflex. Stabilization of a conditional reflex is connected with habituation of the orienting reflex, and all *changes* in the conditional reflex are connected with an increase in activation of the orienting reflex.

As Figure 102 shows, the reciprocal relationship between the orienting reflex and the conditional reflex can be demonstrated. We have obtained similar data in other modalities and with other conditional reflexes, for example, in motor conditional reflexes.

*Lowell:* Why does it take forty-seven trials to elaborate that defensive reaction to the shock?

*Sokolov:* Because, in these experiments there is interaction in the same efferent pathway; the two different reflexes use the same efferent system. In experiments that use different efferent pathways for the two reflexes, a defensive reflex can be elaborated after one or two presentations. But in the experiment presented here, there is competition for what Sherrington called "the final common path." (63).

*Doty:* Is this also true even though you have given the conditioning stimulus many times before, and have habituated this orienting reflex? In other words, you have used this conditioning stimulus for what Szwejkowska (72) calls a "primary inhibitory stimulus."

*Sokolov:* Yes. This is an example of the habituation of the orienting reflex to the shock.

*Doty:* Yes, but not to the unconditioned stimulus.

*Sokolov:* Yes, to the unconditioned stimulus as well, because the first presentation of that shock also produced an orienting reflex.

*Doty:* But isn't it possible that the history of the two stimuli, *i.e.*, their separate application, is responsible for so many trials being needed in order to form the conditional reflex?

*Sokolov:* I believe it is partially connected, because in the study of motor reflexes after habituation of the orienting reflex to the sound, the rapidity of elaboration of a motor reflex is decreased. Similar results have been obtained by Konorski (36).

*Fremont-Smith:* Let me put this in a very simple form, to see if I understand you. If you have habituated two different orienting reflexes which have been presented separately, the fact that they are brought together simultaneously gives you a new stimulus and, hence, a new orienting reflex.

*Sokolov:* That's right. There is novelty in the combination.

*Roberts:* Could there be any effect after habituation if you injected a small amount of norepinephrine, for example, without giving another stimulus—some endocrine effect after habituation had taken place? Would changing the endocrine balance change the response even without the introduction of another type of stimulus?

*Sokolov:* Unfortunately, I have no experience with pharmacological data.

*Roberts:* One of my thoughts was that, after a number of stimuli, you might cause the adrenals to discharge.

*Sokolov:* If one stimulus is reinforced with a shock, and another is not reinforced with a shock, two different stages of elaboration can be recorded. In the first stage of development of the vascular defensive reflex, there is a very generalized influence of the reinforcement upon the conditioned response. But after a number of presentations, a very precise and specific conditioned response is elaborated.

In Figure 103, the magnitude of the vascular response and its duration have been measured and expressed on the ordinate in square millimeters

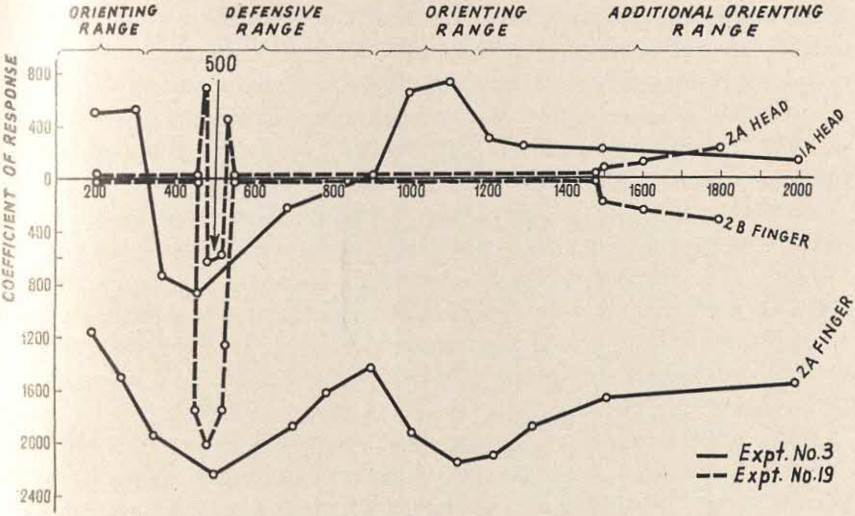

FIGURE 103. Relationship between defensive and orienting reflexes with increasing numbers of reinforcements by shock (500-cps sound). Abscissa: frequency of sound in cps. Ordinate: magnitude of vascular reaction (area under the curve). Vasodilation, upward. Vasoconstriction, downward. By the third experiment (solid lines), the range of defensive conditional reflexes is wide (from 300 to 900 cps). The orienting reflex is evoked by all frequencies within this range. In the course of elaboration, the conditional defense reflex became very specific to the frequency of 500 cps (broken line, Expt. No. 19). The orienting reflex is evoked most strongly by stimuli which are close in frequency to that of the conditioning defensive stimulus. Additionally, orienting reflexes to a range of widely different frequencies develop (right).

(area under the curve). Vasodilation is plotted upward and vasoconstriction downward. The solid lines show the elaboration of the conditional reflex, for the head (upper line) and for the finger (lower line). In every case, the frequency of 500 cps was reinforced by shock.

In the first stage, sounds from 300 to 900 cps evoke a defensive reflex, as evidenced by vasoconstriction in the head (although only a frequency of 500 cps is followed by shock). In frequencies near to this defensive range, there is an increase in the orienting reflex. It is important to note that the orienting reflex is increased in the range of frequencies close to the one used with reinforcement, *i.e.*, to the stimulations which are reinforced by the shock. After a number of trials (Expt. No. 19, broken line), a very specific response develops. The defensive reaction now occurs only in the range between 490 and 510 cps.

With frequencies close to this range, there is a very strong orienting reflex but with more remote frequencies there is no effect, no orienting reflex. Only at an extreme range of frequency, very far from 500 cps, is the orienting reflex evoked again, and then only weakly. When the line for vascular reactions in the head goes above the zero line, it denotes an orienting reflex. When this line goes below the zero line, it indicates a defensive reflex.

The extreme range is itself a novel stimulus. How can these data be explained by the postulated neuronal model system diagrammed in Figure 101? There must be two models: The first is formed for the stimulus which is reinforced by the electric shock; the second is a model for the stimulations which are not reinforced. The orienting reflex is evoked in those cases where a new stimulation does not coincide with one of these models.

If the stimulation is in coincidence with the model for positive reinforcing stimulation, we have as output the defensive reflex without orienting. If the stimulation coincides with the negative unreinforced pattern, no defensive reflex is observed and no orienting reflex.

In the case when the frequency of the stimulation comes between the negative and the positive, the orienting reflex can be very strong and, at the same time, the conditional reflex can be diminished. If the frequency of stimulation is far different from the negative model, no defensive reflex is present, and only an orienting reflex results.

*Doty:* I wonder if you would get the same results if you did not extinguish the orienting reflex prior to starting the experiment. In experiments with cats, in which we did not study the orienting reflex *per se* but rather a part of it, namely, the electrocortical arousal pursuant to the conditioning stimulus, the animals lost this EEG arousal response even though they were shocked each time after this conditioning stimulus. Then, of course, it reappeared as the conditioning came in (8).

*Sokolov:* That is right. If the differential stimulation is different enough from the reinforced stimulation, the negative stimulation produces no orienting and no defensive reflex. However, in the case where the negative and positive stimuli are as close as possible to each other but not in coincidence with either of the two models, we find a range where the orienting responses are very strong. This is a special condition of such a form of experiment. We also have had results similar to yours.

*Leake:* So that we understand each other, is the definition of the orienting reflex based chiefly on changes in blood pressure?

*Sokolov:* No, these are only one of the components of the orienting reflex. I have used them here as an example, because these blood pressure changes enable us to differentiate a specific defensive response and an orienting response. We obtain the same result with another component of the orienting reflex, the $\alpha$-rhythm depression. We have experiments in which the $\alpha$-rhythm depression was compared with a motor reflex (clenching the fist) in man.

*Leake:* I see. Then, the orienting reflex is not based entirely on visceral reflexes, but it also includes skeletal reflexes?

*Sokolov:* As I mentioned before, the orienting reflex includes somatic components in the form of eye movements, body movements, and change of position of the body. There are vegetative responses in the form of changes of respiration, vascular responses, heart rate, and the SGR. There are EEG components, which include $\alpha$-rhythm depression or arousal or the change of driving response of the cortex. There are sensory components, in the form of a change of responsivity of the analyzers and the change of their threshold.

*Leake:* I think that is a much broader concept than American physiologists would ordinarily consider under the term *orienting reflex.* I think, for physiologists, generally, the term *orienting* refers to a change of position in space.

*Doty:* No, that is a righting reflex, which is quite different. I think, if we are going to clarify this point, we should remember that Bard's mesencephalic cats still had righting reflexes or orientation in space, but an orienting reflex of this nature was completely lacking.

*Sokolov:* A similar type of experiment to that which I have just described was conducted as an example of the negative model (Figure 104). In this experiment, one frequency of stimulation, 100 cps, was chosen as the negative stimulus, the subject having been instructed that he must not make a fist when he heard this frequency. For the other frequencies of stimulation, he was instructed to make a fist. This is an experiment in which, instead of acting on the specific stimulus, the subject had to restrain the movement. It is an experiment with the negative model instead of the positive.

In the first experiment (Figure 104 *A*), the SGR showed that there was an orienting reflex to the negative stimulus. A change in stimulation frequency of 500 cps was not discriminated and also produced no motor response at first. Then, after the presentation of higher frequencies and without special reinforcement, a more precise differentiation was elaborated. For example, after the repeated presentation of 100 and 500 cps, the subject responded positively to the 500 cps (Figure 104 *B*). After some more trials, 100 cps as a negative stimulation produced no motor reaction and no orienting reflex. But the stimulation at 400 cps

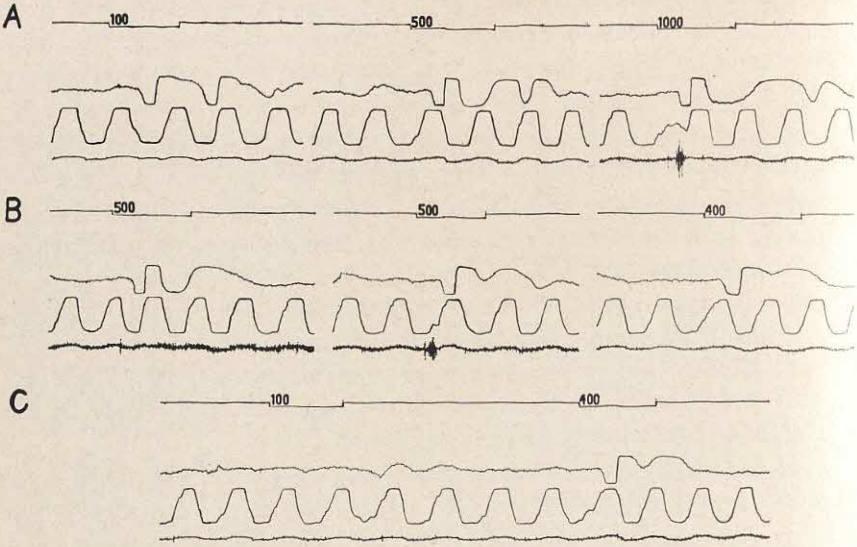

FIGURE 104. Elaboration of a negative conditional motor reflex interpreted by the concept of a "negative model." In (*A*), (*B*), and (*C*), from top to bottom: Sound in cps, SGR, respiration, and EMG of flexors. (*A*) At the start, negative stimulation (100 cps) produced no motor reflexes but a strong orienting reaction. Only a stimulus of very different frequency (1000 cps) produced a motor reaction. (*B*) In the course of repeated comparisons made by the model between negative motor stimulation and stimulation which differed from this, the discriminatory power increased. At first, 500 cps was not effective, but it later evoked a motor reaction. (*C*) On continuation, the negative model became completely inhibiting, and stimulations which differed from it evoked either the orienting (with very close frequencies) or the motor reflexes (with widely different frequencies). Here, 400 cps evoked the orienting reflex without motor reaction.

produced the orienting reflex again without motor reaction (Figure 104 *B*).

Figure 105 gives further examples. At 500 cps, a motor reaction was evoked, and also at 400 cps. The absence of an orienting reflex to 100 cps sound, *i.e.*, the negative stimulus, is observed. With 200 cps, there was only an orienting reflex. Then, after repeated presentation, the same stimulation (200 cps) was discriminated and produced SGR and motor reactions. After further presentations, a frequency of 180 cps was differentiated and produced the orienting reflex. By the end of the experiments, 150 cps produced only an orienting reflex, and 80 cps produced both an orienting and a motor reflex (42).

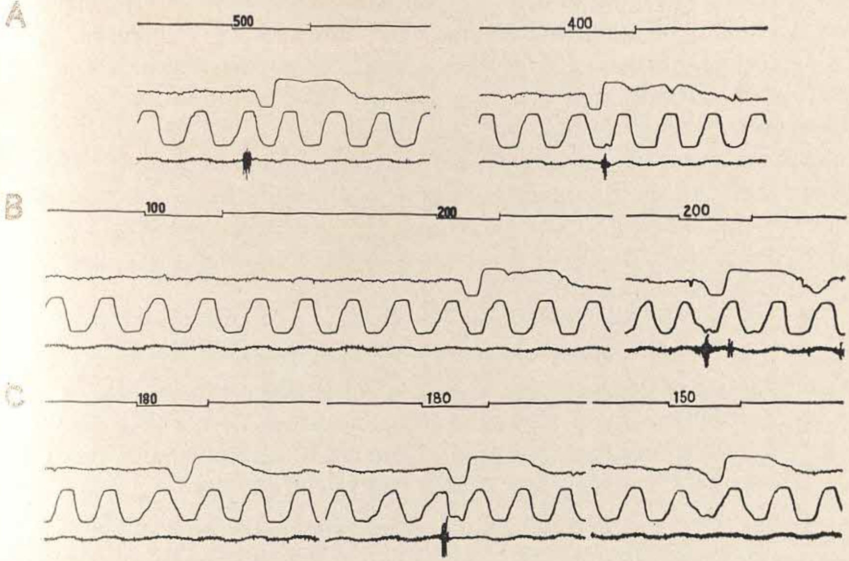

FIGURE 105. Elaboration of negative motor reflexes (continuation of experiments of Figure 104). (*A*) After a number of trials, 400 cps and 500 cps became effective in evoking both motor and orienting reflexes. (*B*) After a number of trials, 100 cps as a negative model evoked no response. Signals near to it in frequency evoked the orienting reflex either alone or combined with the motor reaction. (*C*) At the end of the experiment, 100 cps remained ineffective, 180 cps evoked either the orienting alone, or the orienting and motor reflexes, and 150 cps evoked only the orienting reflex. This experiment shows that the orienting reflex is increased mostly in the range of positive stimuli that lie close in frequency to the negative model.

The negative stimulation produced no orienting and no motor reflex. Then, there was a range where the orienting reflex was increased, without motor reaction. Then, the positive responses with a motor reaction were present. This means that between the negative model and the positive model, there is a special range where the orienting reflexes are increased independently of the motor response. These data are in agreement with those which I showed on the defensive reflexes. The same relationship holds.

From this point of view, it is of great interest to study motor reflexes in conditions in which no neuronal models can be elaborated (70). This was done by using, as the stimulus, a very faint light. With such weak stimuli, the elaboration of a model was very difficult to produce, and in these conditions, no inhibition of the orienting reflex took place.

Figure 106 shows that after several presentations of very faint light, the SGR and α-rhythm depression are very strongly expressed. The stimulation in Figure 106 *A* was a light 2.1 times the threshold for perception administered after 40 minutes of dark adaptation. There was a motor reflex. In Figure 106 *B*, the light was 1.07 times threshold, and there was a very strong response to the weak stimulation. This is called the "threshold orienting reflex." It is an interesting phenomenon that, in the range near the threshold, the orienting reflex is not proportional to the strength of the stimulus. The orienting reflex is greater to stimulations which are very close to threshold.

The same reaction can be observed, in spite of hundreds of presentations. Figure 107 *A* is a very interesting example of the effect of a stimulation a little below the threshold (0.9 times threshold). There is a motor reflex without subjective verbal interpretation of this response. The subject reports that no light appeared and no movement was produced. It is the so-called subsensory reaction (24).

Figure 107 *B* is an example of subthreshold reaction without any motor reaction, only an orienting reflex. Although the latent period of the response is very long, its magnitude and duration are very great. This means that the orienting reflex, in this case, is the reflex response to *lack of information* about the stimulus.

If the intensity of the light is made stronger and presented in com-

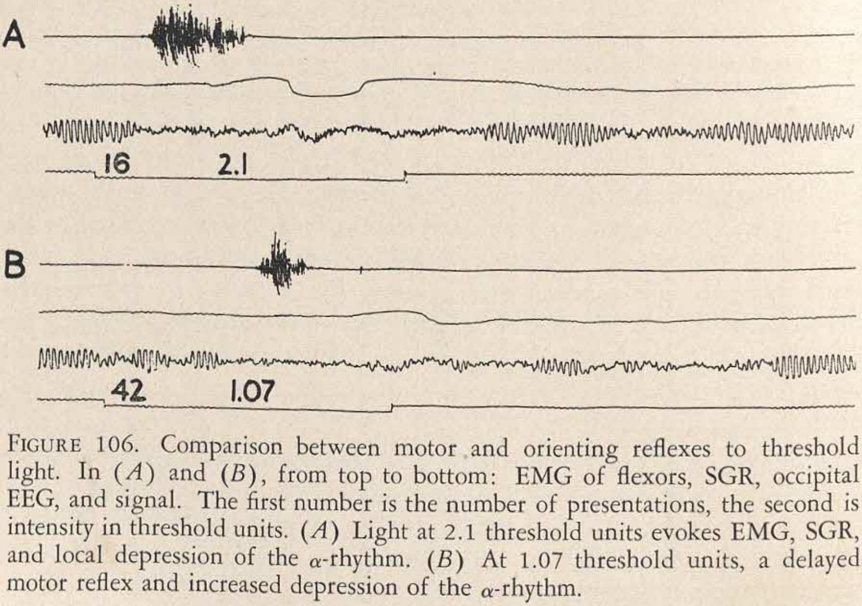

FIGURE 106. Comparison between motor and orienting reflexes to threshold light. In (*A*) and (*B*), from top to bottom: EMG of flexors, SGR, occipital EEG, and signal. The first number is the number of presentations, the second is intensity in threshold units. (*A*) Light at 2.1 threshold units evokes EMG, SGR, and local depression of the α-rhythm. (*B*) At 1.07 threshold units, a delayed motor reflex and increased depression of the α-rhythm.

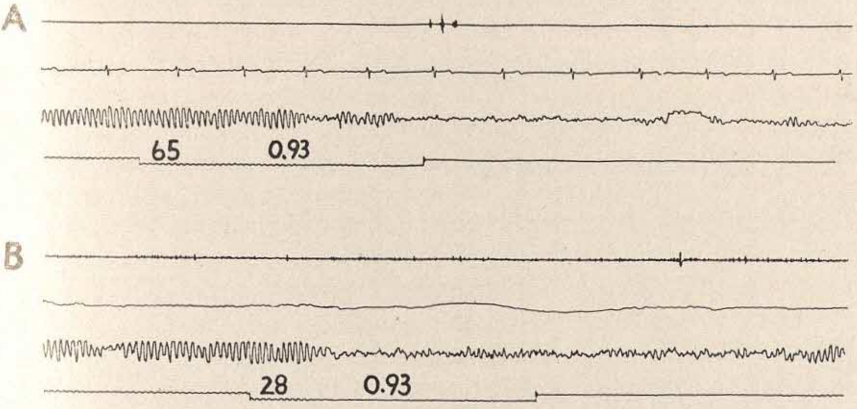

FIGURE 107. Continuation of Figure 106. (*A*) Involuntary motor reaction to a light intensity below the subjective threshold (*i.e.*, tonic contractions in the EMG). Decrease of $\alpha$-rhythm after a long latent period. This pattern of excitation is characteristic of the threshold reaction. (*B*) Response to subthreshold intensity with no motor reaction. The subthreshold reaction is expressed in SGR and in the depression of the $\alpha$-rhythm.

plete darkness, these orienting reflexes disappear after three presentations, but the motor reaction does not. Figure 108 *A* illustrates that with 27 threshold units of light, the motor reflex had a very short latent period; it was a very intensive motor reaction, without generalized orienting, no SGR, but some alpha depression.

In Figure 108 *B* the $\alpha$-rhythm depression is now very slight in spite of the strong motor reaction, and in Figure 108 *C* there is a motor reflex alone. This is an example of the divergence between the orienting reflex and the conditional motor reflex. The presence or absence of these reflexes and the degree of their divergence depend upon the amount of information reaching the neuronal model, and this is determined by the intensity of the stimulus relative to threshold.

*Leese:* Professor Sokolov, I believe I have observed that the design of all these experiments on the orienting reflex is to start with an activity base line of zero. If you should redesign these experiments and the subjects were on a base line of activity, could you still get the same orienting reflexes through?

*Sokolov:* It depends on the reaction being recorded. For example, if a subject is in a state of excitation and the $\alpha$-rhythm is absent with only $\beta$-waves being present, no marked change in the EEG can be observed. But, at this time, the vascular response and the SGR's can

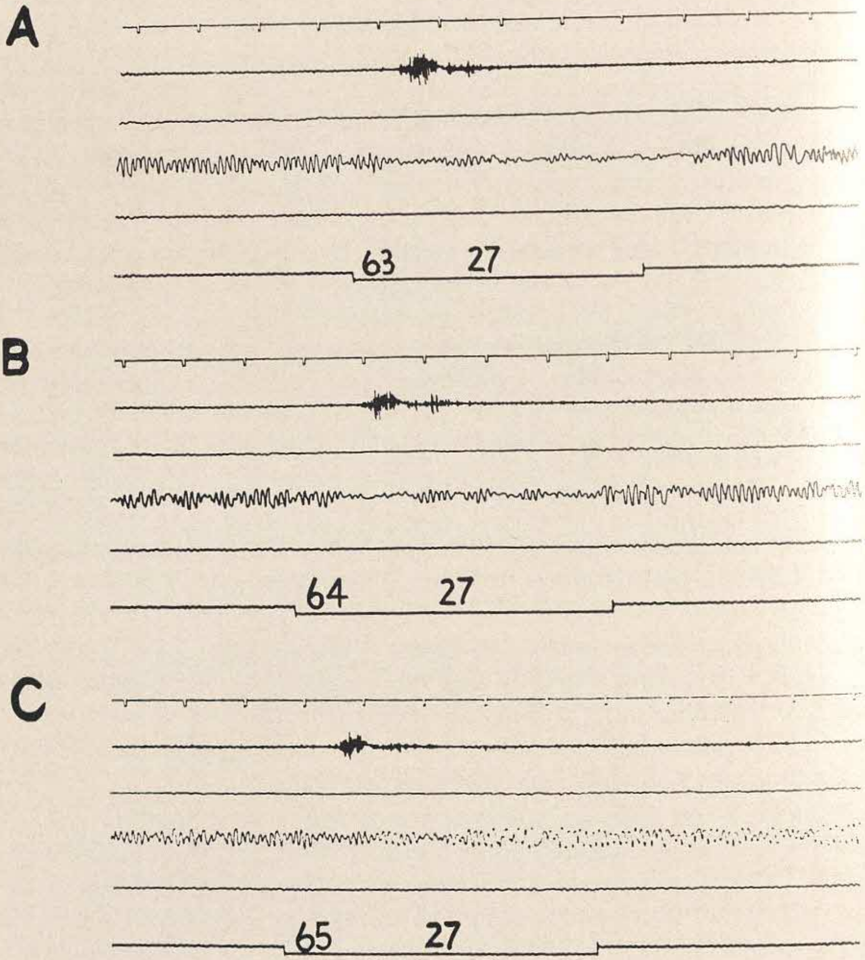

FIGURE 108. Disappearance of the orienting reflex caused by preservation of the motor reflex when light stimuli have become supraliminal. In (*A*), (*B*), and (*C*), from top to bottom: time in seconds, EMG of flexor, SGR, occipital $\alpha$-rhythm, eye movements, and signal for light. The first number is the number of presentations and the second is intensity in threshold units. (*A*) Supraliminal light (27 threshold units) produces a strong motor reaction and decreases the orienting responses. (*B*) The next presentation evokes a strong motor reflex and markedly decreases the orienting reflex as evidenced by the appearance of $\alpha$-waves during the light stimulation. (*C*) The next presentation of the same light evokes a strong motor reflex without any depression of $\alpha$-rhythm. Discrimination of threshold stimuli increases the orienting reflex. This is connected with a difficulty of elaboration by the neuronal model of the changes in the presented stimuli.

nevertheless be very marked. It does not mean that there is an absence of response in the brain, only that we cannot, in this case, observe the changes by the particular method we are using.

*Pribram:* Professor Sokolov, do you have any notion about the differences between the negative model and the positive model and how each is set up in the nervous system; that is, the differences between the defensive and the orienting model?

*Sokolov:* We have information, not about the differences between these models, but about the degree of generalization for positive and negative stimulation. We can, for example, reinforce different stimuli by the same shock. In these experiments, disappearance of the orienting reflex also takes place, because all the stimuli are introduced into generalized models, according to the probabilities of their presentation. Only in the case when just one of the stimulations is reinforced and there is no reinforcement of the other is there a very strong orienting reflex, because, in this case, an additional piece of information about the property of stimulation is obtained.

Figure 109 shows the differentiation between two signals, a positive one of 1000 cps, on which the subject had to press a key, and a negative one of 500 cps, on which he had to refrain from movement. This experiment was made when the subject was in a state of drowsiness as evidenced by the theta waves. In Figure 109 *A*, the positive stimulus was given. The orienting reflex is expressed in the generalized activation in different leads, and in the change of SGR and in a clear motor response. The negative stimulation produced a similar arousal reaction but without the special motor reflex. It is possible to demonstrate this differentiation in conditions of theta wave activity. The model works in these conditions.

We then tried to obtain selective responses to 700 and 1000 cps with the same intensity (30 db) above the threshold for motor response as before. On this background of theta waves, there was a selective arousal to 1000 cps. The only muscle response was a tonic one; the subject did not press the key. Only after the end of this stimulus, when the background activity returned to the stage of $\alpha$-waves, was there a motor reflex. The tonic change in the muscles is a special kind of motor reflex in sleep. It is selective, but it is without actual movement of the hand. It is only a tonic form of subsensory reaction.

*Magoun:* At what point in this series does the subject appear to awaken?

*Sokolov:* In this case, there is no sign of arousal in the motor system. I might mention that sometimes a very interesting phenomenon is seen.

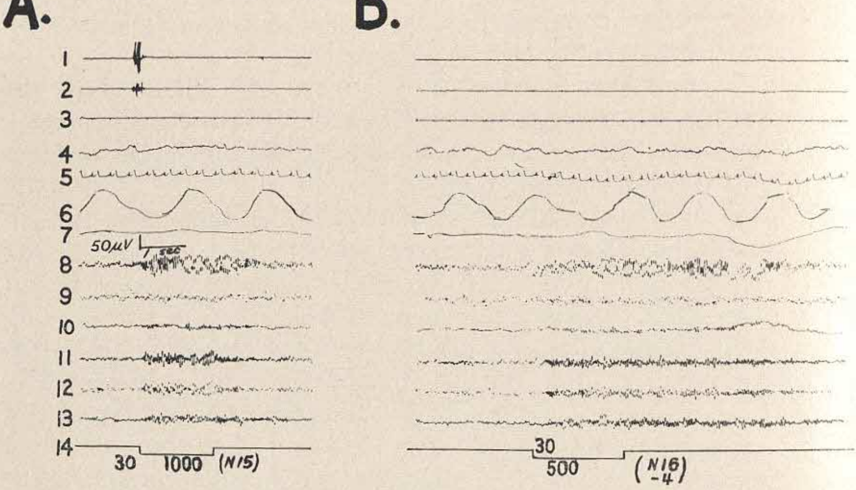

FIGURE 109. Selective motor response and generalized arousal reaction in the first stage of drowsiness in man. 1 = EMG of flexor, 2 = EMG of extensor, 3 = eye movements, 4 = EMG produced by movements of the head, 5 = EKG, 6 = respiration, 7 = SGR, 8 = parietal-occipital EEG, 9 = frontal EEG, 10 = temporal EEG, 11 = precentral EEG, 12 = parietal EEG, 13 = occipital EEG, and 14 = signal (1000 cps, 30 db; 500 cps, 30 db). At this first stage of drowsiness, a positive stimulus at 1000 cps and a negative stimulus at 500 cps both evoke an awakening response ($\alpha$-rhythm, SGR, and respiration). The motor reflex, however, is connected selectively with the positive stimulus of 1000 cps.

We have observed signs of impulses in the motor system without any arousal. It is also interesting that selectivity of the model is present in spite of the slow activity.

*Fremont-Smith:* Professor Sokolov, arousal here, then, means electrical arousal?

*Sokolov:* Not only electrical, but responses in SGR and change in heart rate and respiration as well. The period of respiration is shorter here (Figure 110).

*Bodian:* This would be equivalent to what we call light sleep, because, in terms of the voluntary musculature response, aren't you getting into an area of partial arousal?

*Sokolov:* I can judge only about the stage of EEG sleep. This is a partial arousal which is increased during prolongation of the stimulation.

Figure 111 illustrates the loss of selectivity when there is a background of delta wave activity. Presentation of the same intensity of sound with the same frequency as before (1000 cps) evokes no arousal.

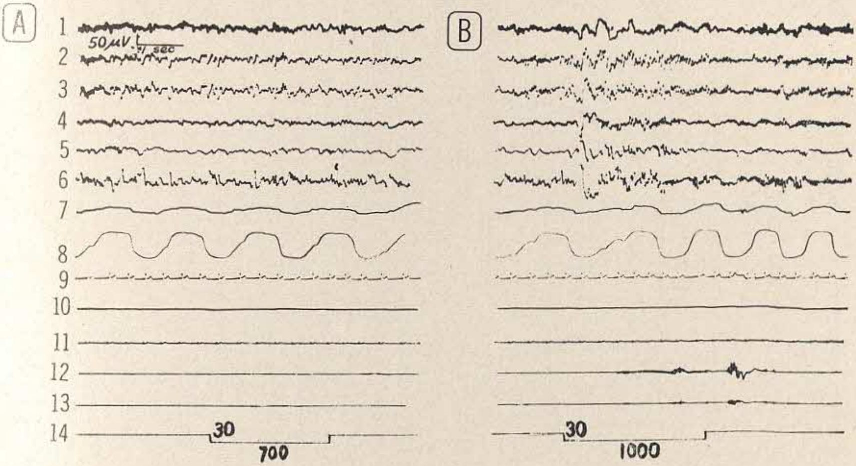

FIGURE 110. Selective arousal to the positive stimulus on a background of theta-wave activity. 1 = occipital EEG, 2 = parietal EEG, 3 = precentral EEG, 4 = temporal EEG, 5 = frontal EEG, 6 = parietal-occipital EEG, 7 = SGR, 8 = respiration, 9 = EKG, 10 = eye movements, 11 = EMG produced by movements of the head, 12 = EMG of extensor, 13 = EMG of flexor, and 14 = signal (700 cps, 30 db; 1000 cps, 30 db). The negative stimulation (700 cps) evokes no arousal in EEG. The positive stimulation (1000 cps) evokes a generalized arousal pattern in EEG (K complex), a change in respiration and pulse rate, and SGR. The motor reflex is a tonic change in the EMG. Only on the background of $\alpha$-rhythm activity, produced by prolongation of the stimulus, does a phasic motor reaction appear. In the stage of theta waves, the selective excitation of arousal response is preserved as a muscle tension without actual movement.

With increase in intensity there is, in this case, after a very great latent period, a tonic reflex in the motor system, a kind of K complex in the EEG and arousal. There is a marked respiratory change and a quickening of the heart rate.

*Fremont-Smith:* Have you used neck-raising?

*Sokolov:* We have, in some experiments. It was found that these responses were not very well expressed. Therefore, we have preferred to use the channels of our recorder for registering the EEG from several different regions of the brain.

*Fremont-Smith:* Does the neck tension come at the same time as that of the flexor?

*Sokolov:* Not in all cases. But sometimes arousal is observed without opening of the eyes, and sometimes arousal without any motor expres-

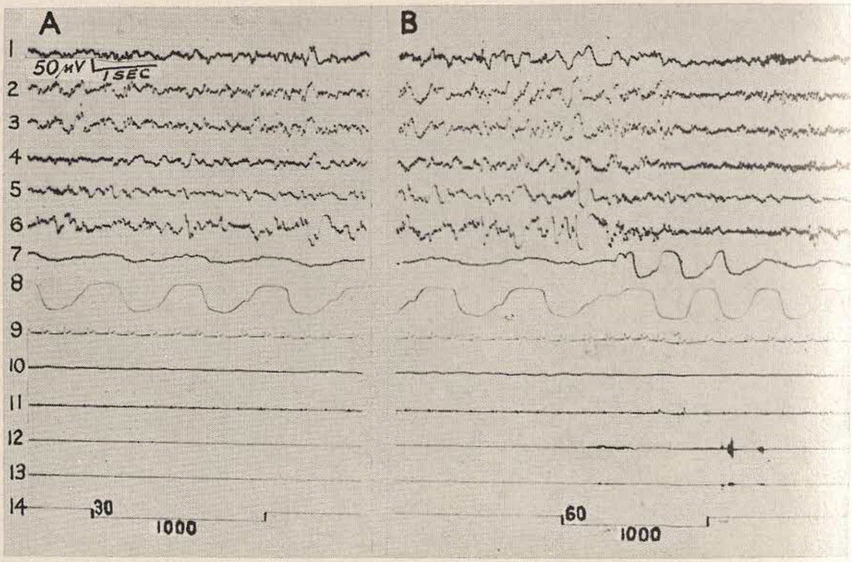

FIGURE 111. Increase of the thresholds of motor reflex and arousal reaction under the influence of delta-wave background activity (see Figure 110). The positive sound (1000 cps, 30 db), which on the background of theta waves produced a selective activation, now with an increase of delta waves, is no longer effective. Only by increasing the intensity of the sound to 60 db does arousal occur in the form of K complex, SGR, and change in respiration and pulse rate. The motor reflex is expressed only in tonic activation with no actual movement. Only with the return of $\alpha$-rhythm, does the subject respond by an active movement. Under the influence of increased cortical inhibition, the selective excitation of arousal and motor reflexes is diminished, and only when an increase of intensity of sound abolishes the delta waves do the motor reflexes return.

sion. Sometimes there is tonic conditioning without subjective knowledge of this fact and without any arousal.

*Leake:* Do you notice any movement of the eyelids?

*Sokolov:* No. It is possible to tell the direction of the movement of the eye from the record, and to distinguish between eye movements and lid-closure. The shape of the response differs. We calibrate beforehand with voluntarily produced eye movements to the right and to the left, and closure of the eyes. Having done this, we can recognize responses.

*Leake:* The reason I asked is that frequently, on awakening, a movement of the eyelids can be noticed before the eyes open.

*Sokolov:* I see. I should say that not in all cases are the somatic components present. Usually the most reactive are the vegetative responses and the EEG.

*Bodian:* Have you worked at this level, or at a somewhat higher level of arousal, with subsequent recall after awakening?

*Sokolov:* There was no recall at this stage. As an additional subject, I might report on the elaboration of conditioning in sleep. The subject just described was one in whom conditioning was elaborated before sleep by a verbal instruction. In some other experiments (57), we studied the elaboration of a passive movement, the passive change of the position of the hand, with sound as the stimulus. In some cases, the subject sometimes reported that he had no desire to press or to change the position of the hand, but that he had pressed involuntarily. In the cases just illustrated, however, there was no verbal reproduction of this part of the response.

*Magoun:* May I extend Dr. Bodian's question to ask if there is any relationship between your work and that of Dement and Kleitman (18) in this country? They awaken individuals when they see changes in the EEG or movements of the eyes of this kind, and then are able to obtain a verbal report of the preceding dreaming associated with this kind of record. Did your subject report any dreaming that might have been related to this kind of record?

*Sokolov:* I do not know the answer, for in our experiments we try not to awaken the subject. Any verbal data have to be obtained after the experiment is over.

*Leake:* What is the number of subjects that you have tested in this way?

*Sokolov:* There were fifteen subjects in the series. It is very difficult to obtain sleep records in conditions in which one stimulation is positive and the other negative. It is much easier when only one indifferent stimulus is used.

*Leake:* Were the responses in the fifteen subjects more or less the same, qualitatively?

*Sokolov:* Yes. It is interesting that when the stage of EEG activity was the same, the responses were also in general the same.

*Leake:* The reason I asked was this: There is some evidence that has been obtained by Petrie (45) on what she calls "intensifiers of sensory stimulations," as opposed to those she calls "reducers of sensory stimuli." This differentiation can be shown particularly with painful stimuli, but it also seems to be associated with other sensations, including sound and light and touch. You ran into no major differences that way, among individuals who would tend to intensify the character of the stimulations as opposed to those who might reduce it?

*Sokolov:* I have no definite observations in this field. I can only tell you that sounds are more effective than visual stimulation.

*Leake:* You used no pain stimulus of any kind?

*Sokolov:* No, we did not use painful stimuli in this series. But in some other types of experiment we have observed the onset of sleep during repeated presentations of electric shock, though the shocks were not very painful.

*Leake:* This difference between subjects who tend to intensify and those who tend to reduce can be shown quite significantly in regard to pain, and I think that many clinicians are fully aware of this kind of picture.

*Sokolov:* We have studied pain sensation in connection with the relationship between the orienting reflex and the defensive reflex, and I can report that during repeated presentations, the orienting reflex disappears and the defensive reflex and pain sensation increase.

*Livingston:* As I understand it, if you repeat the indifferent stimulus, you often reinforce the tendency to sleep. What would happen if you reduced the intensity of the indifferent stimulus until it was very near threshold? I gather you don't get habituation to threshold stimuli. Would an indifferent stimulus near threshold prevent a person from becoming sleepy? Would that prevent your experimental reinforcement of sleep?

*Sokolov:* The threshold of responses is increased under the influence of sleep. Therefore, there are two different mechanisms: one, a drop of responsivity, and two, a selective influence upon the activity. In the case of sleep, the general drop of responsivity means that the thresholds are very high. For example, in the stage of delta waves, only when the sound reaches about 90 db above threshold is the awakening reaction produced, and even then with a latent period sometimes as long as 3 or 4 seconds.

*Livingston:* Assuming you could identify the threshold: if you put the indifferent stimulus near the threshold, would such a stimulus repetition tend to wake the subject, or would it reinforce sleep? Can you identify the new elevated threshold during sleep? Would the lack of habituation to threshold stimuli obtain? In other words, would a person subjected to repeated indifferent stimuli at the new sleep threshold tend to be wakened rather than be reinforced to sleep?

*Sokolov:* During repeated presentation of the same stimulation in the state of sleep, not an activation, but an increase of inhibition is observed. The delta waves are increased. This can be explained by two functional systems of the reticular formation. One is inhibitory in its influence on the cortex and the other is an activating one. The new data obtained by Tissot and Monnier (73) show that whereas high-frequency stimulation of the reticular formation activates the cortex, slow stimulation of the reticular formation produces an increase in the activity of these inhibitory systems. This coincides with data on the change of potassium produced by high and low frequencies (61). Therefore, we can explain these experiments by saying that, in the course of presentation, a kind of conditioning is elaborated which activates this inhibitory system.

*Keller:* But you can obtain electrical wakefulness as well as electrical sleep in the isolated cerebrum that has no access to the reticular formation, *i.e.*, in the absence of the reticular formation.

*Sokolov:* Unfortunately, I have no experimental data on the isolated cerebrum.

*Keller:* An associate of mine, Henry Batsel (6,7), has demonstrated that if the cerebrum is isolated, if the entire midbrain is removed, immediately afterward the cerebrum shows electrical sleep, as shown by Bremer years ago. However, postoperatively, in a chronic preparation, the brain shows electrical wakefulness, but it also shows electrical sleep. Predominantly, it shows wakefulness, as chronicity develops, that is in the complete absence of any reticular formation.

*Fremont-Smith:* Could we ask a little bit more about this fascinating preparation? Is the wakefulness induced by afferent bombardment and does it disappear in its absence?

*Keller:* No, it is spontaneous. He doesn't have any idea of why they sleep or why they wake.

*Magoun:* But you are unable to influence the EEG pattern by light or olfactory stimulation?

*Keller:* That is correct, but, in certain of these preparations, he has cut the optic nerve and removed its afferent input.

*Fremont-Smith:* Do they show any other sign of wakefulness or sleep than the electrical?

*Keller:* No, none whatsoever. It is not an isolated hemisphere; the corpora striata and cephalic portion of the diencephalon remains with the hemispheres. Figure 112 illustrates one type of preparation Batsel has investigated. It shows photographs of three frontal Pal-Weigert sections taken from the series of the same animal. The sections on the left and in the middle show complete serevance of the brain stem through the cephalic pons. The section on the right shows that portions of both cerebrospinal tracts were not cut. Thus, the transection was complete except that the left portions of the pyramidal bundles were

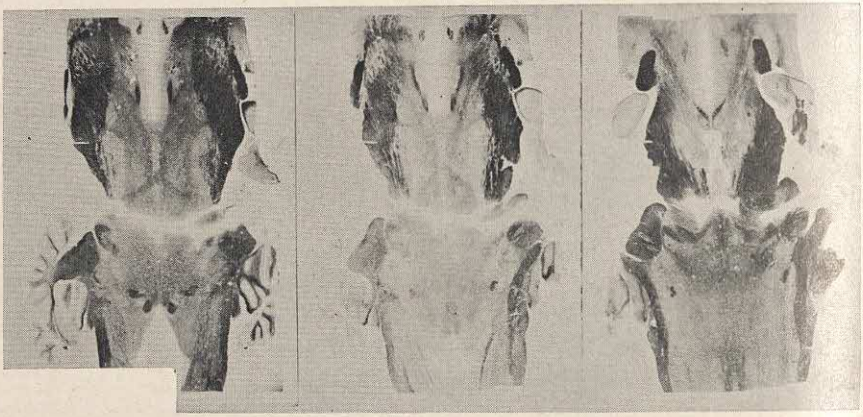

FIGURE 112. Horizontal sections of the brain stem of Dog 661 illustrate the level of transection employed in a series of animals whose EEG's were recorded for several weeks following operation. In this case, bilateral optic nerve section was combined with the prepontine transection without causing synchronization in the chronic state.

spared. Without serial sections, one might miss such an uncut fragment. The brain blocks are cut at 20 $\mu$ and every 20th section is mounted and stained. If and when there is any indication of the transection's being incomplete, all sections through the area under suspicion are mounted and stained. It is important to appreciate that the anatomical structures not involved by the tissue defect remain undisturbed; note particularly that the ventricular system is not enlarged. The tissue ahead is not disturbed. This is just a little farther dorsally. The obex and the third ventricle are visible, as are the fornices going across the middle of the third ventricle, and the mammillothalamic tract.

The tissue defect shown on the photographs of these sections is typical of a transection which produces what I call a *low pontine* or a *high medullary* preparation. Below the transection, the medulla remains undisturbed and above, the midbrain and diencephalon remain with a normal blood supply. I notice that Batsel speaks of this type of transection as producing a *post-collicular* preparation.

The photograph of a sagittal Pal-Weigert section shown in Figure 113 illustrates a second type of preparation, which has been observed by Batsel. In this instance, the tissues of the entire midbrain were aspirated as well as the tissues of the caudal aspects of the diencephalon. Batsel has observed animals in which the aspiration included the entire caudal half of the diencephalon.

They survived for different times. I will now show the electrical

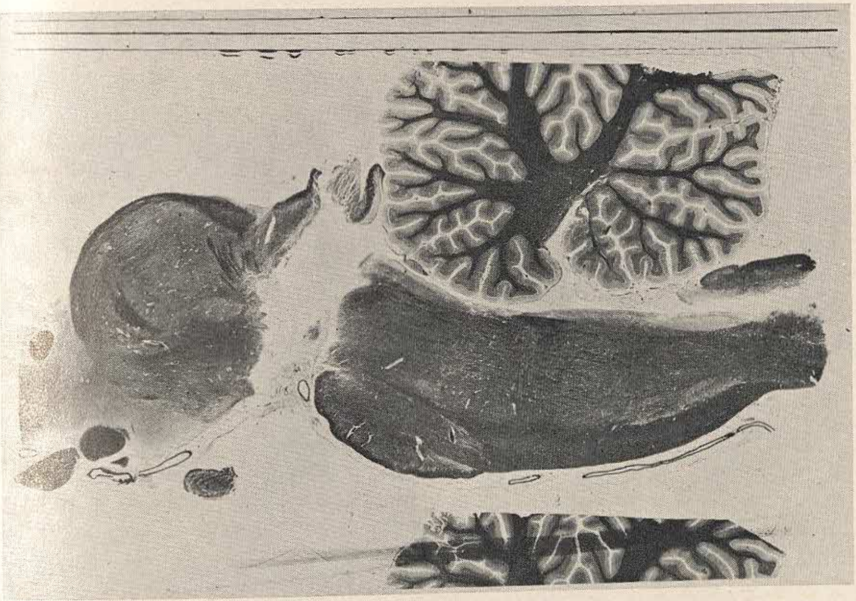

FIGURE 113. Sagittal section of the brain stem of Dog 866. In this case, a large segment of midbrain was removed by aspiration and there was no possibility for ascending conduction into the thalamus. This preparation was maintained for 73 days following operation. Serial EEG's are shown in Figure 115 (see page 244). Reprinted, by permission, from Batsel, H. L.: Electroencephalographic synchronization and desynchronization in the chronic "cerveau isolé" of the dog. *EEG Clin. Neurophysiol.* 12, *421-430 (1960).*

activity of the brain illustrated by the photograph of the section shown in Figure 113. These preparations survive for months, if you wish to keep them that long, except that it is more difficult to keep a preparation after removal of the midbrain than when the transection is accomplished by a narrow tissue defect. This is because there is a much greater incidence of internal hydrocephalus subsequent to the former than to the latter type of operation. The first manifestation of a developing internal hydrocephalus in these preparations is the appearance of a deficiency in the neurohypophysial antidiuretic principle as reflected by a renal concentrating deficit.

I made the remark earlier that Batsel had observed dogs in which the entire reticular formation had been removed. This is true provided that one thinks in terms of the descriptive anatomy of this formation. As I think of the reticular formation, it does not extend cephalad beyond the midbrain or at least beyond the junctional tissue lying between the midbrain and hypothalamus. Thus, the animal I describe as having the

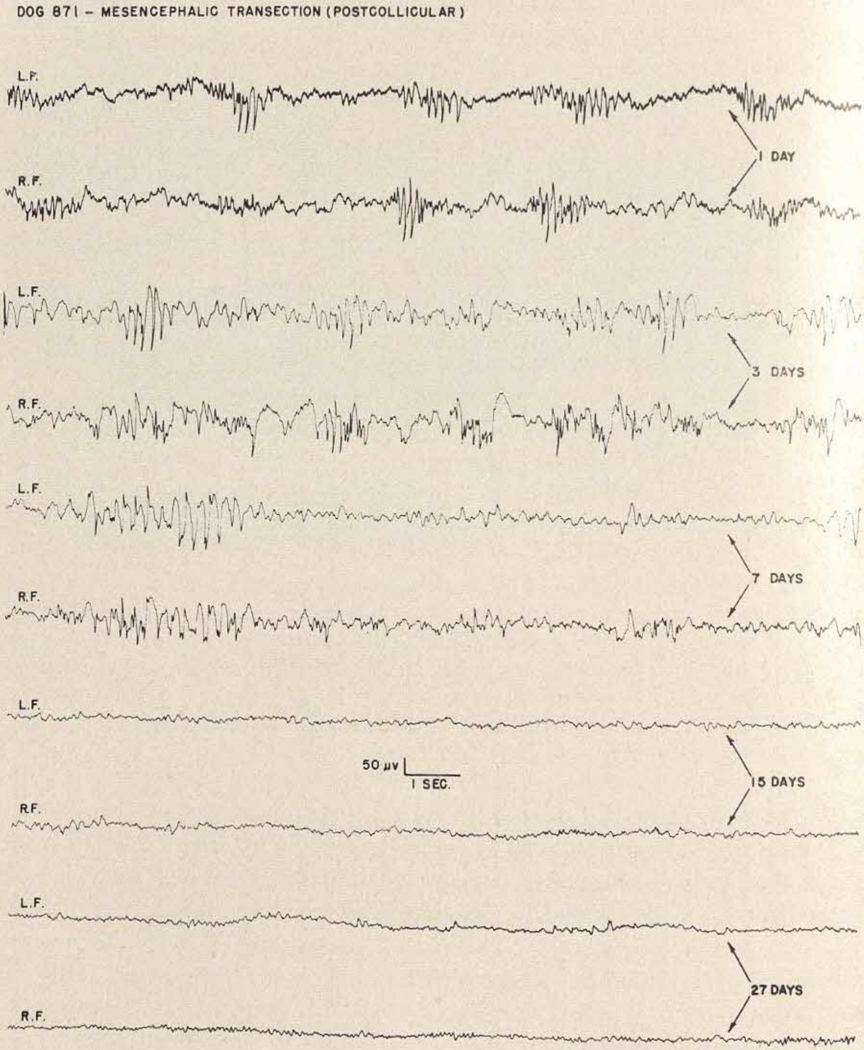

FIGURE 114. Serial EEG's of a low midbrain preparation (ventral tegmentum remained in continuity with the cerebrum). Initially, the EEG pattern showed continuous slow waves and spindles, but from the 15th through the 27th days there were long periods during which there was low-voltage fast activity. Reprinted, by permission, from Batsel, H. L.: Electroencephalographic synchronization and desynchronization in the chronic "cerveau isolé" of the dog. *EEG Clin. Neurophysiol.* 12, *421-430 (1960).*

midbrain removed, lacks the cephalic portion of the reticular formation according to this definition. On the other hand, if one thinks in terms of the "medial activating system," as determined by exploration with electric shocks (artificial stimuli), perhaps a remnant of this system remains, since a varying amount of the cephalic portion of the diencephalon remains in these preparations from which the midbrain has been removed.

Having shown you representative levels of brain stem transections, I shall now show (Figure 114) representative electrocorticograms recorded from such isolated cerebrums and at the same time I will read into the record Batsel's resumé.

"As a cerveau isolé preparation becomes chronic, there is a great probability that the EEG will change from a continuous pattern of synchronization, such as would be expected in sleep, to a prolonged pattern of waking. This is illustrated in Figure 114, which covers a 27-day span following isolation of the cerebrum. Throughout the first two weeks, the EEG pattern was such as would be expected from the classical results of Bremer. Therefore, there were frequent periods during which the EEG was activated as shown here on the 15th and 27th days." Those are the two lower tracings.

*Pribram:* Did these preparations have olfactory and optic nerves cut, too, as you said earlier?

*Keller:* He has had preparations in which the optic nerves were cut. Whether they were cut in this particular one, I do not know. He writes:

"In this particular chronic preparation, there were periods of as much as six hours during which the EEG pattern was continuously activated or flat. However, this spontaneous activation is not a fixed pattern; in fact, this pattern may revert to the typical slow wave and spindle pattern if the EEG is recorded over a sufficiently long session. Sampling indicates that the sleep pattern may reappear for periods of only about one hour out of six in the chronic preparation. Spindles and slow waves may also be induced by appropriately small doses of atropine or barbiturates, and also with chlorpromazine."

Figure 115 shows serial EEGs recorded from the second brain that I showed you.

"This is the animal as it progressed in the acute state from the 1st through the 14th day. Aside from some periodic indication of seizure activity, the records are again those of sleep. This type of pattern persisted for 27 days.

"It will be noticed that there was a more or less stepwise increase in frequency as the animal became more chronic. The length of time

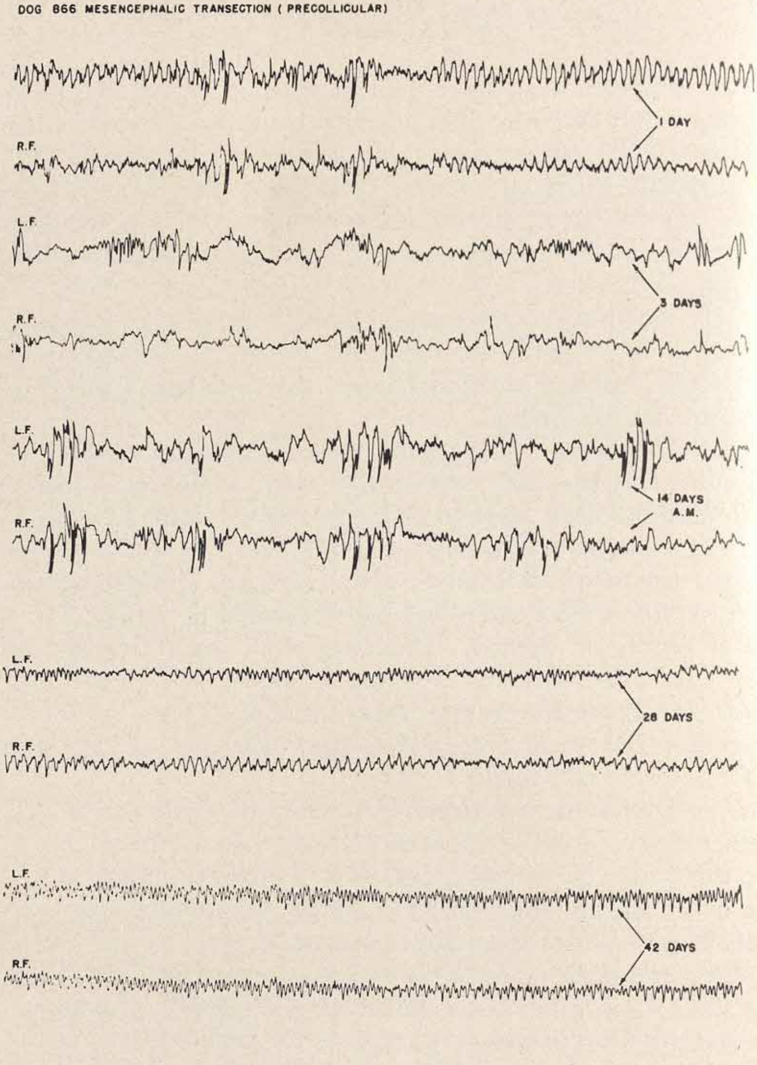

FIGURE 115. Serial EEG's of chronic cerveau isolé preparation, Dog 866. For the first 27 days continuous slow waves and spindles were present except during short periods when seizure discharges obliterated the pattern. Eventually there were long periods of low-voltage fast activity (10 to 30/sec) such as those shown here on the 42nd and 63rd days. Reprinted in part, by permission, from Batsel, H. L.: Electroencephalographic synchronization and desynchronization in the chronic "cerveau isolé" of the dog. *EEG Clin. Neurophysiol.* 12, *421-430 (1960)*.

occupied by activated patterns also increased up to the 58th day, when a pattern similar to this one at the 63rd day was recorded.

"These results indicate that there is an inherent but variable tone, located somewhere within the cephalic extent of the activating system, which remains connected with the cerebral cortex. The optic and olfactory nerves contribute no essential activating tone to this system. The optic nerves have been cut prior to midbrainectomy, and yet the activated pattern develops. Physiologic stimulation through the olfactory system has never sufficed to produce EEG arousal in chronic preparations when synchronized patterns have occurred."

I was in New Orleans very recently, and had a most interesting talk with Dr. L. M. N. Bach at Tulane University, where this matter of consciousness was discussed. We have found, in our experience through the years, that in making any sort of a central nervous lesion, such as a transection or a massive ablation, if a hematoma of any size forms in the tissue defect, the animal dies in a matter of only a few days. We just cannot keep such an animal alive. We have always associated the failure to maintain such animals (aside from nursing care) to a hematoma or a large mass of necrotic tissue.

Dr. Bach was telling me that he has made the same observation in cats, in which he has placed electrolytic lesions—I assume rather sizable ones—in the reticular formation of the midbrain with a Horsley-Clarke instrument, and then subsequent to the destruction of the tissue, he reintroduced a pipette and aspirated the necrotic tissue. He says, as far as consciousness is concerned and postoperative recovery, the preparations differed very remarkably; with association of residual necrotic tissue or blood, particularly blood, in the defect, the animals exhibited evidence of unconsciousness, were comatose. He says that the length of time they remained comatose was directly proportional to this residual necrotic tissue or hematoma.

He also made the remarkable statement that he has, by implanting pipettes into the region, aspirated some tissue in the unanesthetized animal, without momentarily interfering with its consciousness. However, I didn't see the tissue, nor did I learn how much he removed.

I don't know whether or not Dr. Bach has published this. This recalls to mind the paper published by Bailey (4,5), who associated the extirpation of the aqueductal gray with loss of consciousness. I really think, based on my own experience, that Bach has focused attention on a variable that needs to be watched carefully.

*Roberts:* It is not surprising to me that necrotic tissue produces all kinds of effects, because autolytic phenomena occur. We have studied sterile autolysis of brain tissue (56) and a number of amino acids and amines were found to be liberated which are pharmacologically active materials. Reactions take place which ordinarily would not occur *in vivo* because cell components are put in contact with one another which are not normally in contact with each other. From a chemical and pharmacological point of view, therefore, the findings would be entirely understandable.

*Keller:* Yes, and that would be directly associated with the matter of keeping the animals alive. But it would not be associated with this proposition of consciousness, because there would not be time for degradation products to be formed and disseminated into the cerebrospinal fluid or the general circulation.

*Magoun:* I am sure all of us admire the remarkable preservation of these chronically transected animals and their study. They present a fascinating opportunity for the investigation of interrelations between the cerebral cortex and deep structures of the forebrain.

*Keller:* Yes. Of course, the question immediately arises just what do such observations mean physiologically? One definite conclusion is that the completely deafferented cerebrum has the inherent capacity for arousal as judged by the criterion of electrical activity. But there are, of course, a lot of other questions that these observations raise. This delay of a matter of days before electrical arousal occurs intrigues me. It causes one to think in terms of the "spinal shock in reverse" phenomenon, perhaps.

*Windle:* I would like to add something in connection with Dr. Keller's comment on the reticular formation. We have produced confluent lesions bilaterally in the midbrain reticular formation in two monkeys asphyxiated during birth. In one case, the lesion extended caudad to the midbrain formation and, in fact, it went all the way down the spinal cord. These are the only two monkeys in our series that were in prolonged coma. They could not be aroused.

*Magoun:* Did you have a recording from the cortex ahead of the lesion?

*Windle:* This was in the early stages of the work, and our recordings were not very satisfactory. We did make recordings, but I can't tell you what they showed.

*Bodian:* How far forward did the lesion extend?

*Windle:* It included the thalamus.

*Leese:* Professor Sokolov, you have shown the orienting reflex under the influence of single sensory stimulation and under combinations of sensory stimulations in which we have seen facilitation and inhibition, and all the sensory stimulations have been comparatively short in duration. In terms of sensory bombardment, I remember some experiments, years ago, I believe by Wedensky (82), in which he established a condition he called hysteriosis, by a long afferent bombardment. With that particular background, can you still evoke an orienting reflex, do you know?

*Sokolov:* Prolongation of stimulation causes disappearance of the generalized orienting reflex. The local oreinting response is different. For example, we have studied the threshold of the visual system by means of EEG depression to light, using a red pin point of light for fixation of the eye in the dark. We have found that this small red dot, which is present in darkness, can influence the background EEG activity for sometimes 3 to 5 days of experiment. Therefore we had to work to habituate the subject to this before we could begin the experiments with light. So, I blieve that the local orienting reflex can be very stable and long-lasting.

*Bridger:* I have been making experiments on habituation in human newborn babies, and would like to present some of the data (11).* Wee masured the heart rate and behavioral responses when the babies were stimulated by a series of tactile, auditory, and thermal stimuli. Two basis types of responses were observed. The first was a generalized nonspecific startle-like response, perhaps similar to the orienting reflex, and the second was a local specific adaptive type of respose. This is best illustrated by observing a baby's response to an air puff on his abdomen which elicited a generalized startle. The same air puff when applied to the mouth elicited a specific roting or sucking response. We found two qualitatively very different kinds of autonomic response patterns accompanying these specific and nonspecific arousal reactions. Figure 116 illustrates the kinds of responses a 3-day-old baby gives when an air puff to the abdomen is applied for a period of 5 seconds once every minute. Here the change in heart rate produced by the stimulation is correlated with the level of heart rate before stimulation. As you can see, when the baby was drowsy or sleeping, the pre-stimulus heart rate level was low and the heart rate response was high. As he became more and more aroused, the pre-stimulus heart rate increased and the heart rate response was decreased. At a certain point, there was a decrease in heart rate with the stimulation. Perhaps this can be looked at as if the baby's heart rate went to a given, specific level every time the stimulus elicited a startle response from him. His heart rate had to rise quite a

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*This work was supported in part by U.S.P.H.S. Mental Health Career Investigator Grant ♯M2249.

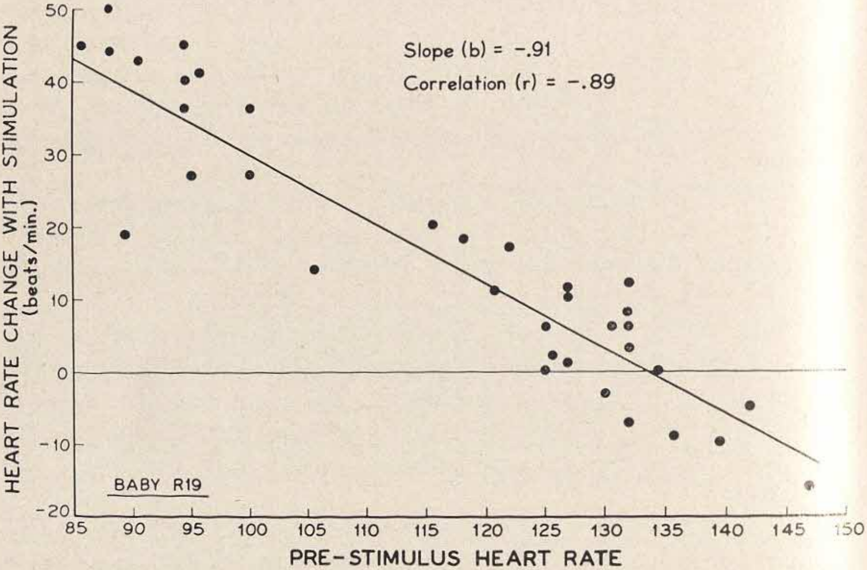

FIGURE 116. The heart rate responses of an individual baby to a series of identical air-stream stimulations of the abdomen plotted against the specific heart rate just prior to each stimulation. The line is a statistical best-fitting regression line for the responses. Reprinted, by permission, from Bridger, W., and Reiser, M.: Psychophysiological studies of the neonate: an approach toward the methodological and theoretical problems involved. *Psychosom. Med.* 21, *265-276 (1959).*

bit when the initial level was low and on the contrary, when his initial level was high, the same startle response was accompanied by a decrease in heart rate. Therefore, the size and direction of the change depended on the heart rate level just prior to stimulation. This is the autonomic response pattern accompanying a nonspecific generalized reaction.

In Figure 117 are the heart rate responses to an air puff stimulation applied to the baby's mouth. I divided the behavioral responses into two classes depending on whether the baby gave a local sucking, rooting or mouthing response or whether he gave a generalized startle response. The round empty circles show the heart rate changes accompanying the startle responses. They are very similar to the air puff on the abdomen. The heart rate response when he gave a rooting or mouthing response was very different for low pre-stimulus heart rate levels; that is, the quieter he was, the smaller the heart rate response and, as he became aroused and excited, he gave a larger response. However, when he became very excited, the air puff not only produced a very vigorous sucking response but also decreased his general over-all activa-

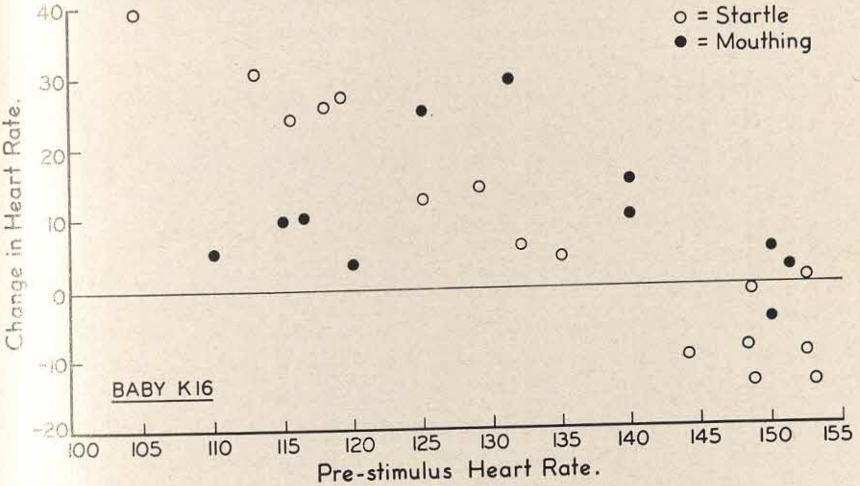

FIGURE 117. A scattergram of the heart rate responses of an individual baby to a series of air-stream stimulations in the oral zone categorized as to the accompanying behavioral response—a nonspecific general activation or a local specific response. The patterning of the heart rate changes accompanying the startle response is similar to that seen in Figure 116. The heart rate changes accompanying the mouthing responses resemble an inverted U-shaped-pattern.

tion and the accompanying heart rate response started to decrease, and thus conform to the so-called "law of initial value." The same type of inverted U-shaped curve results as that which Duffy (19) and Malmo (40) described as a typical arousal pattern.

There are, then, two kinds of responses: One, the nonspecific so-called orienting or startle response which is independent of the state of the baby. The baby always tends to go to the same level when stimulated and this is the "law of initial value." Two, the specific local response which, like the sucking response, depends on the state of the baby. The quieter he is, the smaller the response, and as he becomes more excited, the bigger the response.

*Purpura:* Are your subjects all newborn babies?

*Bridger:* They are all less than 5 days old. They vary between 1 and 5 days. When we repeated this tone, we varied it. We studied the parameters of this habituation by making behavioral observations and measuring heart rate. The duration of the stimulus varied from 5 seconds to sometimes 20 or 30 seconds, and the interval between the stimuli was as short as a half second and as much as 20 or 30 seconds. Let me just show you the results.

## TABLE IV

## Parameters of Sensory Habituation

| Baby L43 | | Pure Tone 40 cps | | | | | |
|---|---|---|---|---|---|---|---|
| Duration 20 sec Interval 10 sec | | Duration 5 sec Interval 5 sec | | Duration 5 sec Interval 3 sec | | Duration 20 sec Interval 5 sec | |
| 1. +++ | 16. + | 1. +++ | 16. + | 1. ++ | 16. — | 1. +++ | 16. + |
| 2. ++ | 17. + | 2. ++ | 17. + | 2. +++ | 17. + | 2. ++ | 17. + |
| 3. +++ | 18. + | 3. +++ | 18. + | 3. +++ | 18. — | 3. ++ | 18. — |
| 4. +++ | 19. + | 4. +++ | 19. + | 4. ++ | 19. + | 4. ++ | 19. + |
| 5. ++ | 20. ++ | 5. ++ | 20. — | 5. + | 20. — | 5. +++ | 20. + |
| 6. ++ | 21. ++ | 6. +++ | 21. — | 6. — | 21. — | 6. + | 21. + |
| 7. + | 22. + | 7. +++ | 22. + | 7. + | 22. — | 7. + | 22. + |
| 8. +++ | 23. — | 8. ++ | 23. + | 8. ++ | 23. — | 8. + | 23. + |
| 9. + | 24. + | 9. — | 24. + | 9. + | 24. — | 9. — | 24. — |
| 10. + | 25. + | 10. + | 25. + | 10. + | 25. — | 10. ++ | 25. — |
| 11. ++ | 26. — | 11. + | 26. + | 11. — | 26. — | 11. + | 26. — |
| 12. + | 27. + | 12. — | 27. + | 12. + | 27. — | 12. + | 27. — |
| 13. ++ | 28. + | 13. + | 28. — | 13. ++ | 28. — | 13. + | 28. — |
| 14. + | 29. + | 14. + | 29. + | 14. + | 29. — | 14. + | 29. — |
| 15. — | 30. + | 15. — | 30. + | 15. + | 30. — | 15. + | 30. — |

The ratings of behavioral responses of an individual baby to a series of constant pure tone auditory stimulations. The ratings are pooled from three independent observers and were as follows: +++ = full startle, ++ = modified startle, + = any behavioral evidence that the baby heard the stimulus, — = no behavioral change with stimulation. The duration is the length of time the stimulus is on, or being applied, and the interval is the length of time between stimulations.

As Table IV demonstrates, in the first instance, the duration of the stimulus was 20 seconds with an interval of 10 seconds. We found that the habituation of the arousal response had two phases. Whether they are identical with the ones described by Professor Sokolov and by Sharpless and Jasper (62) is open to conjecture, but the first event was a tremendous startle response which quickly habituated out in eight to ten responses. From then on, we just listed whether the babies gave any responses as rated by three independent observers.

It turned out that when the duration of the tone is 20 seconds, with an interval of 10 seconds, the baby continued to respond, and almost all babies continued to respond, to many more than 30 repetitions of the stimulus. When we decreased the duration of the stimulus to 5 seconds, with an interval of 5 seconds, the babies also did not habituate completely. When they went through this first habituation, they stopped giving the startle response but continued showing some behavioral manifestation.

Then, when we decreased the interval to 3 seconds, with a duration of 5 seconds, we found that we could get habituation, at which the baby stopped responding to the specific auditory stimulus. The babies also habituated in that way when the duration was increased with an interval of 5 seconds, that is, when there was an interval of 5 seconds and a duration of only 5 seconds, they did not habituate. When we increased the duration of the stimulus to 20 seconds, we found habituation, also.

This has been studied in over fifty babies, and our general conclusion is that the habituation process depends on how long the stimulus is applied and on the interval between the stimuli. The shorter the interval, the easier it is to get habituation, and the longer the stimulus, the easier it is to get habituation.

One of the ways of checking this habituation is to increase the interval once the baby has habituated. When the baby habituates, shall we say, to an interval of 5 seconds, if we increase the interval between the stimuli to 8 seconds, the baby starts responding again. We found differences between individual babies, which seem to be reliable and might reflect some sort of fundamental organismic temperamental difference between these babies related to their ability to habituate to stimuli. We also found that when we changed the frequency, as Professor Sokolov mentioned, we got the startle response immediately.

Figure 118 shows the heart rate and the behavioral response. We stimulated the baby with a tone at a frequency of 400 cps. We went through eighteen trials to attain habituation and found that the average stimulus heart rate was down to 104, with no behavioral response. We

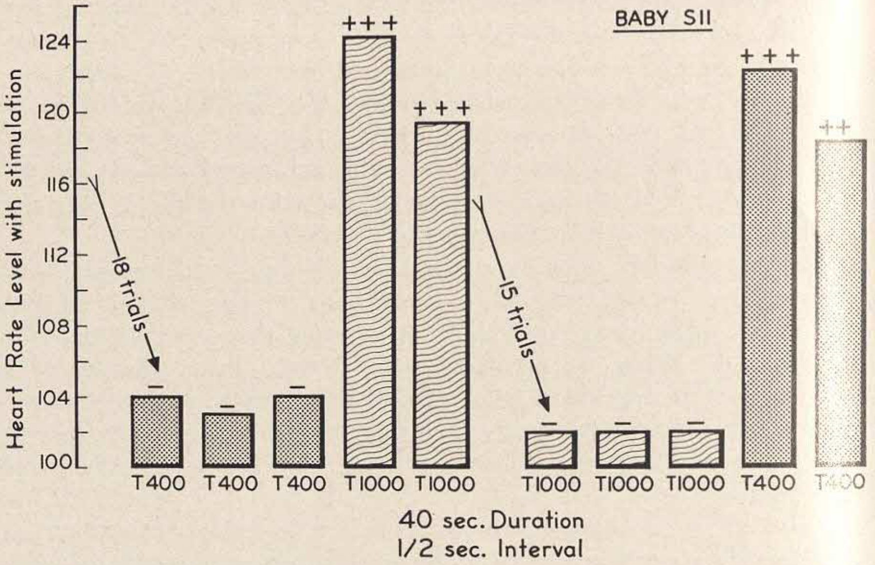

FIGURE 118. Pitch or auditory frequency discrimination in a 2-day-old infant. The heart rate response is indicated by the level of heart rate reached during the first 5 seconds of stimulation. The behavioral responses shown above the bars, are rated as in Table IV. The trials indicate the number of consecutive stimulus applications necessary for complete habituation. Three additional trials were given after habituation occurred and before the switch to the novel stimulus.

repeated this specific stimulus three times, with no behavioral response. We used the same interval in order to be sure we got good habituation. This was half a second, and the duration was 40 seconds.

When we switched to a new tone of 1000 cps, we got the startle response again with the increase in heart rate. After fifteen trials, it started to decrease. The baby was not responding to this tone at 1000 cps. We continued this for three more trials, and then, when we switched back to tone 400 cps, we got the startle all over again. Not all babies show this process of habituation and discrimination process; however, most do show habituation, especially when we make the interval as short as ½ second. But, out of forty babies, only twenty showed this kind of discrimination. Some babies were very good in their so-called discriminatory capacity, and one baby was able to discriminate between a tone of 200 and a tone of 250 cps. He was a newborn baby.

*Magoun:* Is this a corticifugal process? The cortex of the newborn infant is thought to be in an exceedingly immature functional state.

*Bridger:* I don't think this clarifies that question any more than Sharpless' and Jasper's studies on decorticated cats do. I don't think any babies did better than Sharpless' decorticated cats (62), so I really can't say. Whatever question that experiment dealt with, this just goes along with it.

I would say that in dealing with Professor Sokolov's neuronal model, there are two different levels of habituation and two different areas where these occur. For a certain complex differentiating kind of comparison, the cortex is needed. The discrimination found in neonates is more likely a primitive physiological process, because, as you can see, the habituation is limited; that is, the intervals between stimuli are very short and the baby's ability for habituation is limited when compared with Professor Sokolov's experiments.

An interesting by-product of this was the experimental induction of sleep. By continuing a stimulus for a long period of time, such as 40 or 50 seconds, the baby would assume a catatonic-like attitude and would no longer respond. This very loud tone is a very efficient way of quieting babies.

We also found that this induction of sleep is dependent upon the intensity of the stimulus. With a stronger stimulus, the inhibition is stronger and more immediate.

*Purpura:* One of the points I should like to take up immediately relates to the question of what we mean by immaturity of the cerebral cortex. For example, is the word "immaturity" to be used in a global sense or are there distinct differences in the rate of maturation of different types of cortex and different synaptic organizations? To answer this question, my colleagues, Dr. Carmichael and Dr. Housepian, and I initiated a series of experiments in near-term fetal and newborn cats (49). We focused our attention on the anatomical and physiological development of two fundamentally different types of cerebral cortex, *i.e.*, neocortex and archicortex. The first three figures summarize the salient histological features of the neuronal architecture in the developing neocortex and the developmental state of hippocampal neurons at birth in the cat. It should be mentioned that our Golgi-Cox material was obtained from the same animals in which physiological studies were carried out.

Figure 119 *A* shows a cluster of medium and large pyramidal neurons in the suprasylvian gyrus of the newborn cat. This preparation was 5 hours old at the time the physiological studies were initiated. The cat, like the rat, rabbit, and human infant, is immature when born. It should

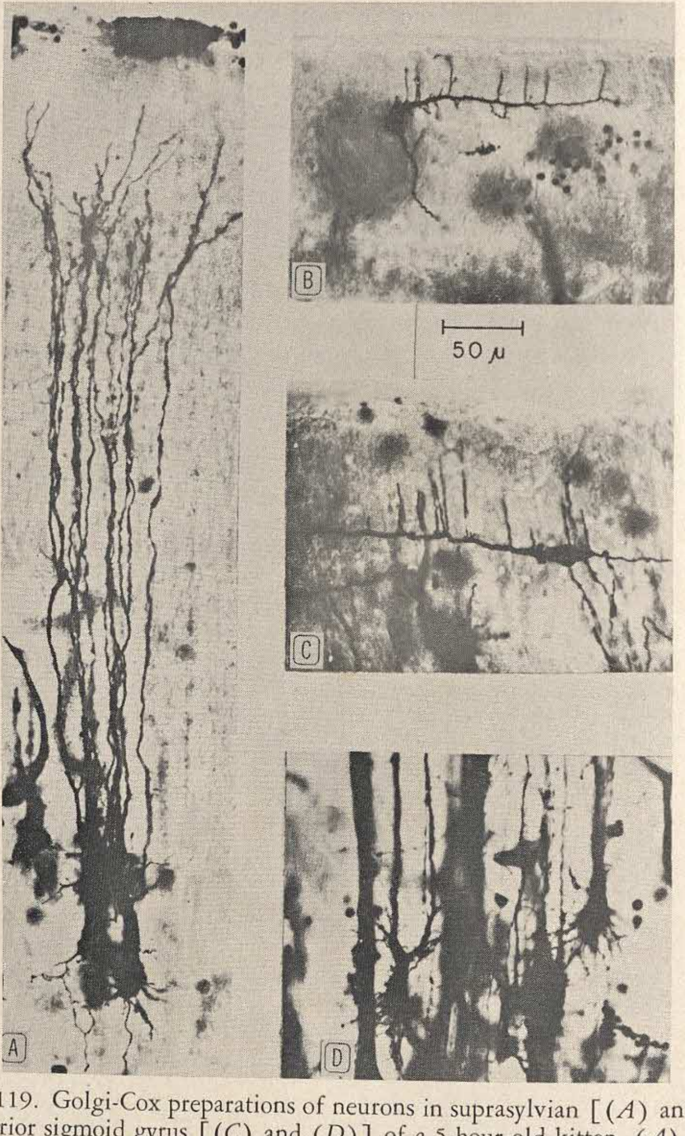

FIGURE 119. Golgi-Cox preparations of neurons in suprasylvian [(*A*) and (*B*)] and anterior sigmoid gyrus [(*C*) and (*D*)] of a 5-hour-old kitten. (*A*) Cluster of medium and large pyramidal neurons. Apical dendrites extend to within 25 to 50 μ of pial surface. Note absence of lateral branches. Axons of two neurons clearly shown extending downward. Basilar dendrites at this stage are short, thin processes. (*B*) and (*C*) Embryonic Cajal-Retzius neurons in molecular layer. (*D*) Giant pyramidal neurons in motor cortex with massive apical dendrites but poorly developed basilar dendritic system. Same magnification in all photomicrographs. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

be recalled that eye-opening in the cat occurs about 9 to 11 days postnatally.

Medium and large neocortical pyramidal neurons have well-developed apical dendrites at birth in the cat, but are relatively devoid of basilar dendrites. Axons are also well-developed, but few recurrent collaterals are detectable. Some small and medium pyramidal neurons in the submolecular layers appear to possess basilar dendrites which may extend 3 to 5 times the cell body diameter.

Neocortical pyramidal neurons in the newborn cat resemble in many respects those in the newborn human infant, as shown in Conel's (17) studies. However, it appears that the development of the basilar-dendritic system in the newborn human neocortex is somewhat more advanced than in the newborn cat.

Figure 119 *A* also shows the presence of small bulbous dilations on the distal segments of apical dendrites, but no thorns, spines, or gemmules are seen at birth in the cat.

The molecular layer of neocortex contains a large number of Cajal-Retzius cells (Figure 119 *B* and *C*) in addition to the apical dendrites of pyramidal neurons and tangential fibers from deeper regions. These neurons have characteristics which are identical with those observed in the newborn human infant (17,53). Dendrites of these cells generally course tangentially for varying distances (50 to 200 $\mu$) in the middle and lower third of the molecular layer. Emerging at right angles to these tangential elements are numerous radially oriented branches which terminate near to or at the pial surface. Such right-angle branches may be spaced as closely as 5 to 10 $\mu$ apart and arise from small varicosities on the tangential elements. Distinctions between axons and dendrites of these cells are often difficult to establish. Some of their identifiable axons intertwine with densely packed apical dendrites of pyramidal neurons and may be followed for 100 to 200 $\mu$ before they are lost in a maze of apical dendrites. Cajal-Retzius cells undergo "regressive changes" by the 5th to 8th postnatal day, which eventually result in the loss of the numerous radially oriented dendritic ramifications characteristic of the perinatal period. Cajal (53) and Conel (17) note that the "regressive" changes are completed by the end of the first month in the human infant.

One further point concerning the development of neocortical apical dendrites at birth in the cat: the proximal portions of the apical dendrites are of considerable thickness relative to cell body diameter (Figure 119 *A* and *D*). Branching of middle and distal segments is minimal, but when this occurs, radial orientation of branches is maintained. Long tangential branches of apical dendrites in their proximal or middle segments have not been observed at birth in the cat, although a few delicate processes less than 50 $\mu$ are occasionally discerned in small superficially located pyramidal neurons. Apical dendrites extend into the molecular layer where large numbers of them, densely packed, terminate within 25 $\mu$ of the pial surface. Others appear to end in contact with the latter. Tangential spread in the molecular layer of apical dendrites of medium and giant pyramidal cells is rarely greater than 100 $\mu$, but some small superficially located neurons give rise to apical dendrites, the tangential branching of which, in the molecular layer, may occasionally approach 150 to 200 $\mu$.

The growth of basilar dendrites of medium and large pyramidal neurons appears to gain momentum within a few days after birth and by the 3rd postnatal day numerous short elements (50 to 75 $\mu$) of small caliber relative to cell body diameter begin to arborize extensively (Figure 120 *A*). An accelerated phase of basilar dendritic growth occurs during the early part of the 2nd postnatal week (Figure 120 *B*). By the end of the 3rd postnatal week, long basilar dendrites are seen in all neocortical areas (Figure 120 *C*). In contrast to the profound development of basilar dendrites in the postnatal period, apical dendrites undergo relatively little proliferation. Apart from changes in volume, these elements rarely have tangential branches in the molecular layer that are longer than 150 to 200 $\mu$, as Sholl (65) has shown in the adult cat. By the end of the 3rd to 4th week, it appears that cat neocortex has reached the mature state. Dendritic spines are discernible on about the 8th postnatal day and after the 3rd week they are well-developed as shown in Figure 120 *C*. During the first 2 weeks, there are rather striking changes in the internal architecture of pyramidal neurons, as revealed by Nissl stains, but these will not be considered at this time.

Comparison of neocortical pyramidal neurons (Figure 119 *A* and *C*) with hippocampal pyramidal neurons (Figure 121) reveals that in the newborn cat the latter have attained a degree of differentiation that is usually not seen in neocortical pyramidal neurons until after the 10th day. It is clear from this that in speaking about maturation of the mammalian cerebral cortex one must be aware of the striking differences in the rate of maturation of phylogenetically different types of cortex.

To turn from histological to physiological considerations, the problem arose as to whether the maturational difference in the cytoarchitectural organization of neocortex and hippocampus was reflected in physiological differences. To explore this problem, studies were initiated

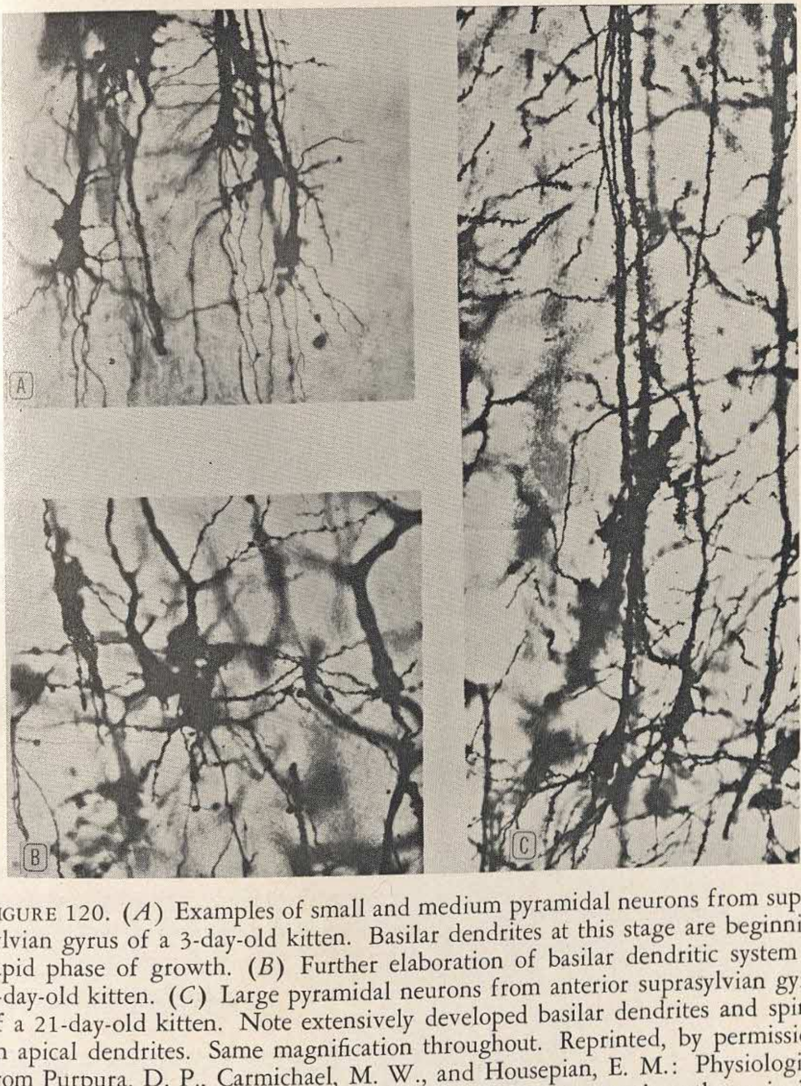

FIGURE 120. (*A*) Examples of small and medium pyramidal neurons from suprasylvian gyrus of a 3-day-old kitten. Basilar dendrites at this stage are beginning rapid phase of growth. (*B*) Further elaboration of basilar dendritic system in 8-day-old kitten. (*C*) Large pyramidal neurons from anterior suprasylvian gyrus of a 21-day-old kitten. Note extensively developed basilar dendrites and spines on apical dendrites. Same magnification throughout. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

on the changing properties of synaptic organizations in superficial neocortical neuropil during the first month. A small number of experiments were also performed on near-term fetal cats delivered by Caesarean section. In all the experiments to be described, techniques similar to those employed in adult cats were utilized in order to make comparisons

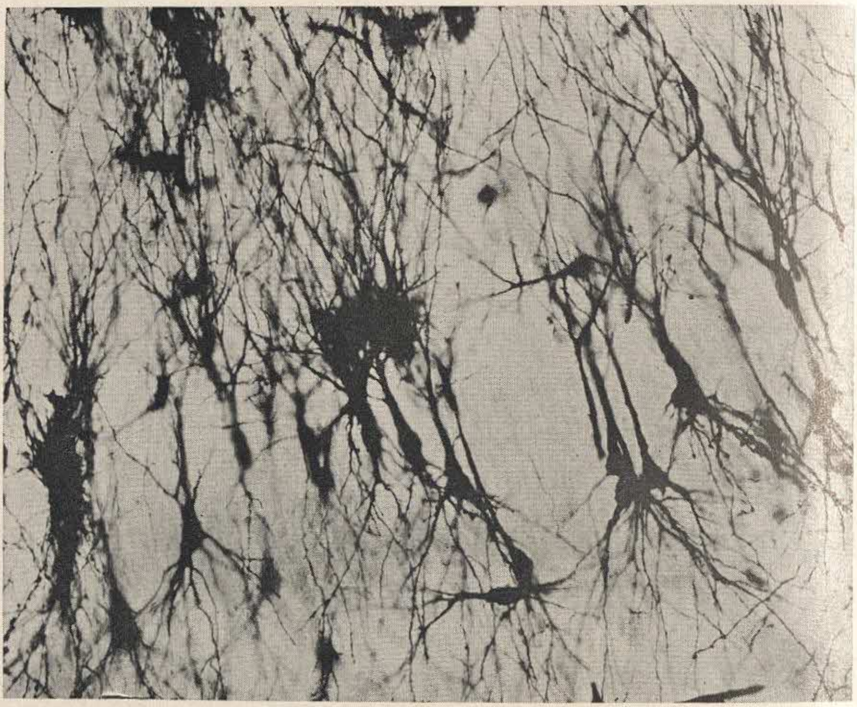

FIGURE 121. Hippocampal pyramidal neurons from a 15-hour-old kitten. Extraordinary development of basilar dendrites (below) as well as apical dendrites (above) is clearly shown (x220).

with data obtained from the mature animal (50,51). Kittens were anesthetized with ether to permit introduction of a tracheal and an external jugular vein cannula. After completion of all operative procedures, skin margins were infiltrated with procaine and the kittens were allowed to recover, then paralyzed with succinylcholine chloride and artificially ventilated.

The electrographic characteristics of the superficial cortical responses to local stimulation of suprasylvian gyrus are shown in Figure 122. In near-term fetal and newborn cats, SCR's recorded 1 to 2 mm. from stimulating wire electrodes exhibited typical graded characteristics to stimuli of progressively increasing strength. It is unusual to detect much late positivity except with stimuli of very great magnitude. Some peculiarities were noted, however, which have not been described in the adult animal (1,14,16). The first relates to the extraordinary duration (50 to 80 msec.) of the SCR in newborn cats when recorded under conditions identical with those in which 10- to 20-msec. responses are

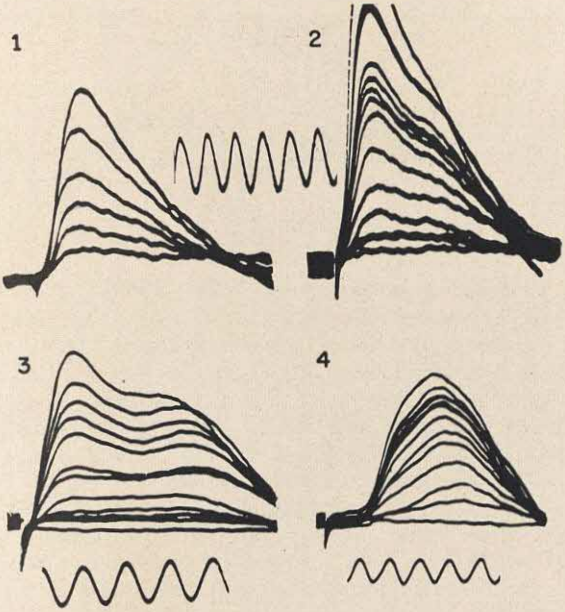

FIGURE 122. Characteristics of long-duration superficial cortical responses recorded 1.5 mm. (*1* to *3*) and 4 mm. (*4*) from stimulating electrodes on supra sylvian gyrus. Stimulus frequency 0.5/sec; 6 to 20 superposed responses at different stimulus strengths. Negativity upward in this and all subsequent figures. *1* and *2* from two near-term fetal kittens; *3*, 4-day-old kitten; and *4*, 12-hour-old kitten. Duration of SCR's independent of stimulus strength; threshold of late components in near (*3*) or distant (*4*) responses similar to that for the early components. Latency of distant responses is not appreciably altered by 5- to 10-fold increase in stimulus strength. Note augmentation of early component in near responses and late components of distant responses with strong stimuli. Calibrations: 100 cps; 0.1 mV. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

observed in the mature animal. SCR's recorded at sites beyond 2 mm. are of similar duration but later components in the overt responses have a lower threshold than the early ones (Figure 122, *4*). This can also be seen in responses recorded 1 to 2 mm. from the site of stimulation (Figure 122, *3*).

The relationship between near and distant SCR's evoked in two near-term fetal preparations is shown in Figure 123. A stimulus evoking a minimum near SCR also produced a small response 4 mm. away after an appreciable latency (Figure 123, *1*). This latency was unchanged

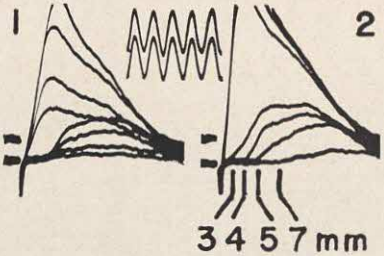

FIGURE 123. Relationship between near (upper channel) and distant (lower chanel) responses in two near-term fetal kittens. *1* = Graded responses at near (1.5 mm.) and distant (4 mm.) sites from stimulating electrodes. Stimulus evoking small near SCR produces detectable distant response after 15-msec. latency. (Propagation velocity: 0.27 M./sec.) *2* = Characteristics of distant SCR's to strong stimuli evoking maximal near SCR's. Note progressively increasing latency of distant responses. (Mean propagation velocity: 0.25 M./sec.) Calibrations: 100 cps; 0.1 mV. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

even with very strong stimuli. In Figure 123, *2,* stimuli were employed which evoked large near responses. In the lower channel traces, responses are shown recorded at 3, 4, 5, and 7 mm. The progressive change in latency with distance is clearly shown. The data indicate that even in the near-term fetal cat responses may be detectable up to 5 to 7 mm. from the site of stimulation. The propagation velocity of the SCR in perinatal preparations was about 0.3 M/sec.

*Leake:* When you get to 7 mm. there is no response?

*Purpura:* There was a small response detectable at 7 mm. in the near-term fetal animals.

In view of the relatively long duration of the SCR in the neonatal cat, the question arose whether this was due to something peculiar about dendritic postsynaptic potentials (p.s.p.'s) in the immature cortex. That this was not the case is shown in Figure 124. In this experiment (5-hour-old cat), the SCR was recorded as previously, 1.5 mm. from the stimulating electrodes (upper channel), and a second electrode of smaller caliber (0.1 mm.) was placed virtually in contact with the stimulating wires (lower channel). Under these conditions, a distinct 10- to 12-msec. SCR was recorded "at the site of stimulation" (Figure 124, *1*). With slightly stronger stimuli, the initial component of the SCR increased in amplitude and there appeared on its falling phase a second and third surface-negativity of 10- to 20-msec. duration. Occasionally, the second

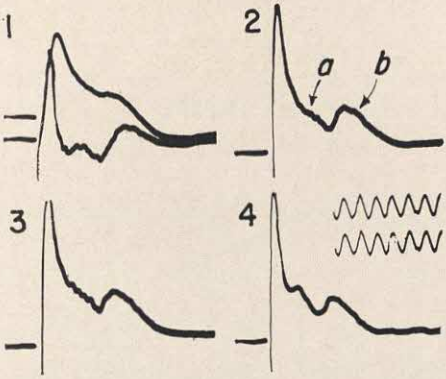

FIGURE 124. Comparison of SCR recorded at 1.5 mm. with a large (0.5 mm.) ball-tipped electrode (upper channel) and SCR recorded "at the site of stimulation" with a 0.1-mm. wire electrode in a 5-hour-old kitten. *2* to *4*, wire electrode at same position, stimulus strength increased to reveal development of late components *a*, *b*. High-frequency oscillation (*a*) an inconstant finding in perinatal preparations. Calibrations: 100 cps; 0.1 mV. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

surface-negativity developed out of a variable series of high-frequency oscillations (Figure 124, *2a* and *3*). The relatively long duration of the SCR in neonatal cats, as recorded under conditions similar to those in which 10- to 15-msec. responses are observed in the mature animal, appears, therefore, to result from summation of a series of 10- to 20-msec. "unit" p.s.p.'s of dendrites. One explanation as to why responses recorded beyond 1 mm. of the site of stimulation are compounded of a number of 10- to 20-msec. p.s.p.s may be sought in the extraordinary density of apical dendrites and dendrites of Cajal-Retzius cells in the molecular layer of neocortex in the newborn animal. During development, this density decreases, owing to the growth of nonneural elements and the fact that the dendrites of Cajal-Retzius cells undergo regressive changes. As noted earlier, apical dendrites grow in length but otherwise there is very little change in the number of apical dendritic branches per neuron.

Another characteristic of the changing properties of axodendritic synaptic pathways in superficial neocortical neuropil is demonstrated in Figure 125. Two series of activity cycles are shown in Figure 125 *A* in a 5-hour-old cat. Conditioning and testing stimuli of equal magnitude were employed. When these were delivered 5 msec. apart, no increment

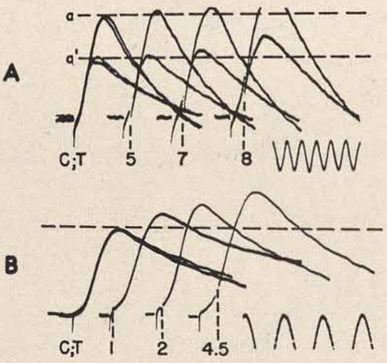

FIGURE 125. (*A*) Early phase of SCR activity cycle in a 5-hour-old kitten. Recording electrode 1.5 mm. from stimulating electrodes. Two series are shown at different strengths of stimulation. The conditioning *C* and testing *T* responses in each series were of equal magnitude. The broken lines *a'* and *a* are drawn through the peaks of responses evoked by weak and strong pairs of stimuli, respectively. The first records in each series show *C* and *T* responses in isolation superposed. Thereafter, *C-T* intervals are as indicated. No increment in conditioning SCR is detectable at 5 msec. *C-T* stimulus intervals in either series. At slightly greater intervals, a small increment in conditioning SCR is observed. (*B*) Early phase of SCR activity cycle in a 7-day-old kitten. Recording electrode 2.0 mm. from stimulating electrodes. First records in series show equal *C* and *T* responses in isolation superposed. Broken line drawn through peak of these responses. When *C-T* interval is 1 msec., a significant increment in conditioning SCR is detectable. With a 4- to 5-msec. *C-T* interval, recovery is greater than that obtaining at 8 msec. in a 5-hour-old kitten (*A*). Calibrations: 100 cps; 0.1 mV. in (*A*); 1.5 mV. in (*B*). Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

in the conditioning response was detectable. Indeed, a slight increment in the conditioning SCR was observed only with 7- to 8-msec. stimulus intervals. A different activity cycle was observed in 5- to 7-day-old animals (Figure 125 *B*). In these, the absolute unresponsive period was reduced to 1 to 1.5 msec., *i.e.*, a distinct increment in the conditioning response was detected with stimulus intervals less than 2 msec. Although considerable variability was found from one animal to the next, in general, by the 3rd to 5th day the absolute unresponsive period in the early phase of the SCR activity cycle was about 3 msec., and by the end of the 1st week it was less than 2 msec.

The change in SCR activity cycles during the 1st postnatal week is also associated with two additional changes which may be noted. It will be recalled that in Figure 123, it was pointed out that although

SCR's could be detected up to 5 to 7 mm. from the site of stimulation in perinatal animals, distant responses were never found to be of greater magnitude than those recorded 1 to 2 mm. from the stimulating electrodes. By the 8th to 10th postnatal day, an entirely new phenomenon is observed. This is shown in Figure 126. In this series of records from

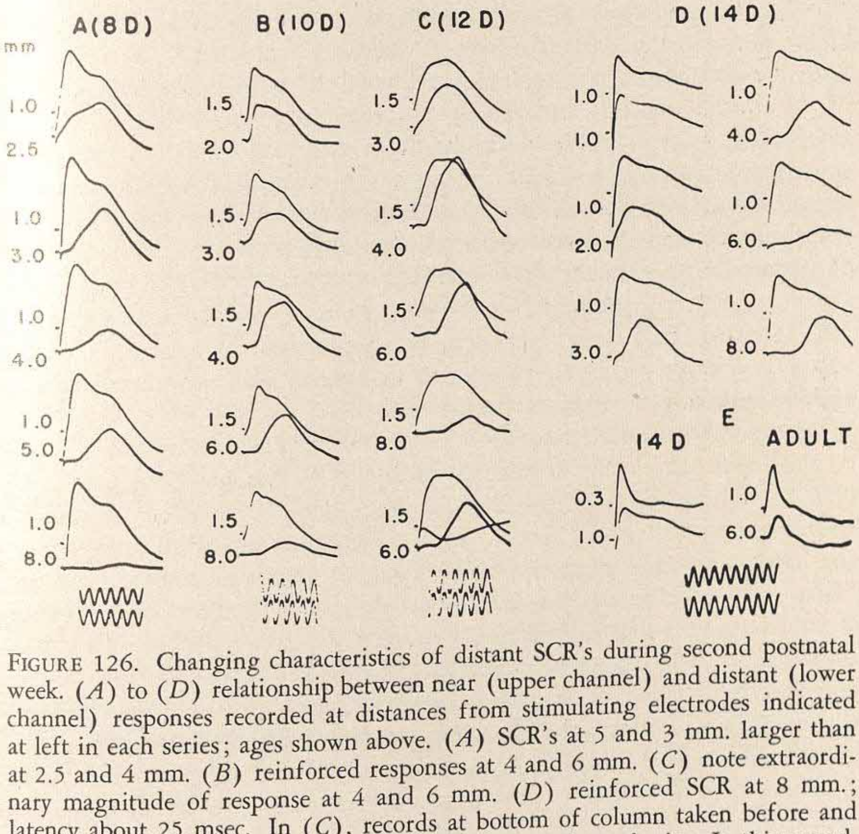

FIGURE 126. Changing characteristics of distant SCR's during second postnatal week. (*A*) to (*D*) relationship between near (upper channel) and distant (lower channel) responses recorded at distances from stimulating electrodes indicated at left in each series; ages shown above. (*A*) SCR's at 5 and 3 mm. larger than at 2.5 and 4 mm. (*B*) reinforced responses at 4 and 6 mm. (*C*) note extraordinary magnitude of response at 4 and 6 mm. (*D*) reinforced SCR at 8 mm.; latency about 25 msec. In (*C*), records at bottom of column taken before and after topical application of 1 per cent GABA to near electrode site. In this record, upper channel shows abolition of surface-negativity and "unmasking" of surface-positivity after GABA; lower channel shows two perfectly superposable "distant" responses. (*E*) comparison of responses at indicated distances in a 14-day-old kitten and adult cat studied under identical conditions. Wire electrode (0.1 mm.) employed to record response at 0.3 mm. in kitten. Compare characteristics of responses at 1 mm. Duration of the distant response in adult preparation is similar to that of near response. Calibrations: 100 cps; 0.1 mV. in (*A*); 0.3 mV. in (*B*) to (*E*); that for (*D*) shown in (*E*). Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

animals of different ages, SCR's were recorded close to the site of stimulation and simultaneously at different remote sites. In the 8-day-old animal, responses recorded at 5 mm. were larger than those recorded at 4 mm. In the 10-, 12- and 14-day-old preparations, distant responses were often of greater magnitude than those recorded 1 to 1.5 mm. from the site of stimulation. This phenomenon, termed "reinforcement" by Brooks and Enger (12), has been studied by them in adult cats. Its appearance during the early part of the 2nd postnatal week coincides with the most rapid phase of expansion of the basilar dendritic system of pyramidal neurons and the development of axon collaterals. The reinforced responses are undoubtedly attributable to temporal and spatial summation of axodendritic p.s.p.'s. Figure 126 illustrates another important property of SCR's. The bottom records in column C show near and distant responses recorded before and after topical application of $\gamma$-aminobutyric acid to the *near recording site only*. GABA eliminated the near SCR and produced some unmasking of surface-positivity (48, 50), whereas the distant response was completely unaltered. This study supports the view that the processes of spread and generation of the SCR are entirely separate events (20,51).

Before taking up the question of the relative development of neocortical and hippocampal synaptic pathways in the newborn cat, mention should be made of the usefulness of data obtained in this ontogenetic study in clarifying some of the problems involved in interpreting the origin and nature of the SCR. First, as regards the origin of the SCR, there is little need to restate the arguments in favor of assigning it to the activity of superficially located dendrites (47). The data obtained in the immature cat indicate that SCR's recorded close to the site of stimulation have similar properties to those recorded up to 8 mm. distant. Such distant responses are conducted along the surface at a mean velocity of 0.3 M/sec. in the neonatal cat and about 0.5 M/sec. in 2- to 3-week-old animals. Linear changes in latency with distance are characteristically observed. In view of the histological findings that apical dendrites in immature cortex do not branch tangentially in the molecular layer beyond 50 to 100 $\mu$, it cannot be maintained that the SCR is both generated in and conducted along dendrites for several millimeters (14). Furthermore, the fact that elimination of near responses by GABA does not alter far responses is added proof that the SCR is generated at successive sites in apical dendrites by conductile pathways in the molecular layer. A reasonable explanation of our data is that a surface stimulus excites horizontal fibers in the molecular layer which generate p.s.p.'s in apical dendrites and dendrites of Cajal-Retzius cells. If descending axon-collaterals from tangential fibers establish effective contact with basilar dendrites and cell bodies of neurons in submolecular regions during the second postnatal week, relayed activity in recurrent axons from these elements may generate p.s.p.'s in apical dendrites which summate with earlier ones evoked at different sites in the same population of dendrites by the more direct tangential pathway. It should be emphasized that temporal and spatial summation of axodendritic p.s.p.'s is markedly enhanced during the phase of rapid expansion of the axon-collateral and the basilar dendritic system of pyramidal neurons.

The fact that axodendritic synaptic pathways in the superficial neocortical neuropil are well-developed at birth in the cat suggests that these pathways may play a role in the elaboration of some behavioral activities in the immediate neonatal period. Such a remarkable differential development of superficial axodendritic pathways may explain the differences in the electrographic characteristics of primary somatic sensory (59) and visual (27) evoked responses in the newborn and mature animal. The prominent initial surface-negativity of these evoked responses in the newborn animal might be a reflection of the underlying difference in the nature of the activity evoked in cortical neurons by primary thalamocortical pathways. It is of further interest to note that in our more recent studies it has been found that low-frequency stimulation of mid-line and anterolateral thalamic regions in the newborn cat evokes prominent surface-negative recruiting potentials which, unlike those observed in the mature animal, do not appear to be compounded of a large intracortical positivity. This again seems to emphasize the extraordinary functional capacity of neocortical superficial neuropil in the newborn cat.

A few examples will suffice to illustrate the differences in the functional capacity of some neocortical and hippocampal synaptic pathways at birth. In Figure 127, the effects of repetitive stimulation in a newborn cat of the neocortical surface and fimbria are compared. The SCR is markedly depressed during and for some time after repetitive stimulation. Whether this represents a rapid exhaustion of transmitter, desensitization of the postsynaptic membrane to the transmitter, or something else cannot be decided.

Recovery of the SCR after repetitive surface stimulation was not complete even after 20 to 30 seconds (Figure 127, *3*). After completion of these studies, the neocortex overlying the hippocampus was removed by gentle suction and recording electrodes were applied to the ependymal surface of the hippocampus. Stimulation of the fimbria evoked a com-

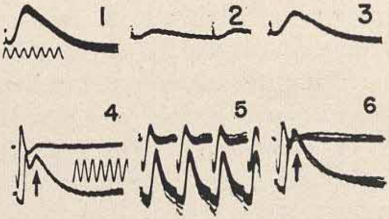

FIGURE 127. Comparison of effects of repetitive stimulation of neocortical surface (*1* to *3*) and fimbria (*4* to *6*) in an 8-hour-old kitten. *1* = Distant (4 mm.) SCR recorded from suprasylvian gyrus, stimulus frequency 0.5/sec. *2* = Depression of SCR during 12/sec. stimulation. *3* = Residual depression of SCR evoked by 0.5/sec. stimulation. Depression persisted for 20 to 30 seconds. *4* = Upper channel, responses recorded from fimbrial-hippocampal junction following 0.5/sec. stimulation of fimbria. Stimulating-recording electrodes about 2 mm. apart. Lower channel, recording electrode on surface of hippocampus, approximately 6 mm. distant from stimulating electrode. The conducted response is succeeded by a longer duration negativity (arrow). *5* = Repetitive stimulation (25/sec.) causes reduction of conducted response and marked depression of postsynaptic event. *6* = Post-tetanic facilitation of component, indicated by arrow in *4*, is clearly shown. Stimulus frequency 0.5/sec. Calibrations: 100 cps; 0.1 mV. Reprinted, by permission, from Purpura, D. P., Carmichael, M. W., and Housepian, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).

plex response from the hippocampus which consisted of an initial spike-like component followed by a longer duration negativity (Figure 127, *4*). During tetanization, some reduction in the amplitude of the conductile response occurred. At the end of a short period of tetanization, responses evoked every 2 seconds were significantly augmented for many seconds (Figure 127, *6*). The fact that hippocampal evoked responses exhibit post-tetanic facilitation at birth in the cat suggests that "immature" archicortex has characteristics which are similar to those seen in the mature animal. This is further indicated by the findings that long-chain aliphatic $\omega$-amino acids which augment evoked responses and induce repetitive convulsant discharges in the hippocampus of the mature animal (48,52) also produce convulsant effects in the hippocampus of the newborn cat. Neocortical evoked responses are not augmented by the convulsant $\omega$-amino acids until about the 3rd postnatal week (13). A comparison of the effects of $\epsilon$-amino caproic acid, the $\omega$-amino acid with two more carbons in the aliphatic chain than GABA, on neocortical and hippocampus responses in the same preparation is shown in Figure 128. This figure also illustrates the effects of topically applied GABA in the newborn cat. Of particular importance is the

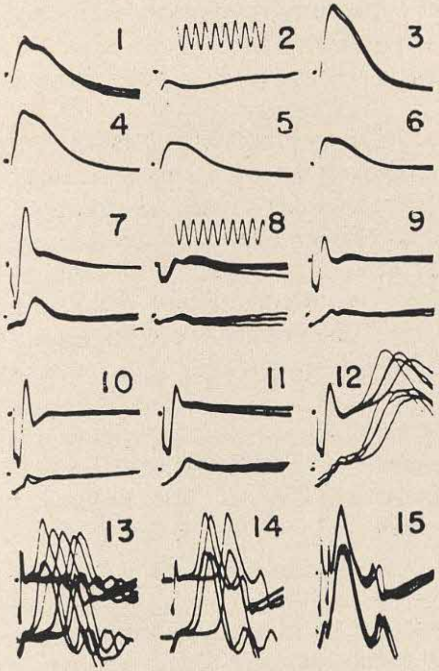

FIGURE 128. Comparison of effects of ω-amino acids on neocortical (*1* to *6*) and hippocampal (*7* to *15*) evoked responses in newborn cat. *1* = Control SCR from suprasylvian gyrus. *2* = 1 min. after topical application of 1 per cent γ-aminobutyric acid. *3* = Recovery after rinsing cortex with warm Ringer's. Note post-GABA augmentation of SCR (50). *4* = Control. *5* = 1 min. after topical application of 1 per cent ε-amino caproic acid. *6* = Continued depression 10 minutes after rinsing cortex with Ringer's. *7* = Hippocampal evoked responses to fimbrial stimulation. Upper channel, surface recording from fimbrial-hippocampal junction; lower channel, surface recording from region of hippocampus corresponding to $CA_1$-$CA_2$. *8* = 1 min. after topical application of 1 per cent GABA. Note depression of conducted response in fimbria and abolition of response recorded from $CA_1$-$CA_2$. *9* = Partial recovery after rinsing away GABA with Ringer's. *10* = 20 min. after *9*. Stimulus intensity increased. *11* = Immediate effect of topically applied ε-amino caproic acid; *12* = 2 min after *11*. *13* = Slow sweep recordings during stage of convulsant activity as in *12*. Conditioning responses in *13*, testing responses in *14*. *15* = Synchronization of convulsant discharges with paired stimulation of fimbria. Calibrations: 100 cps; 0.1 mV. in *1* to *12*. 10 cps in *13* to *15*.

finding that GABA eliminates the SCR but reveals little surface-positivity in the perinatal period (Figure 128, *2*). Following recovery from the GABA-action, ε-amino caproic acid was applied (Figure 128, *5*). This resulted in a depression of the SCR which persisted even after repeated rinsings of the recording site with warm Ringer's solution. In the mature animal, neocortical SCR's recorded close to the stimulating electrode are rapidly augmented by topically applied $\epsilon$-amino caproic acid (50).

The effects of GABA on hippocampal evoked responses to fimbrial stimulation in the newborn cat were somewhat surprising in that 1 per cent GABA had a considerable depressant action on the conducted response in the fimbria (Figure 128, *8*). We have not as yet determined whether this effect of GABA is specific for $\omega$-amino acids. We have, however, established that this depressant action is not observed in immature cats after the 2nd postnatal week. Suffice it to say that in the mature animal GABA does not alter the conducted response in the fimbria (52).

Topical application of $\epsilon$-amino caproic acid resulted in an augmentation of late components of the hippocampal evoked responses and the production of convulsant discharges. The random nature of the late discharges could be eliminated with paired stimuli (Figure 128, *13 to 15*).

The foregoing physiological, pharmacological, and histological data indicate that, in the cat, maturation of different synaptic organizations and phylogenetically different types of cortex proceeds at different rates. This suggests that when speaking about "immaturity" of the central nervous system care should be taken to define the particular synaptic pathway under consideration. This brings up a number of problems concerning the interpretation of biochemical data on the maturation of the brain in which whole brain samples are employed in the analyses of different constituents. When samples of neocortex and archicortex are combined, biochemical differences between the two are likely to be completely obscured.

Finally, the striking developmental differences in neocortex and archicortex in the neonatal period raises a number of questions relating to the role of these phylogenetically different types of cortex in early conditioning responses. However, these are problems which can now be subjected to detailed exploration, and further speculation seems unwarranted. I would like to make one more point, if possible, to illustrate something that tends to be overlooked in talking about maturational changes in the cerebral cortex. Figure 129 is taken from Ramón y Cajal (53). It shows the extraordinary development of the dendritic ramifications of Cajal-Retzius cells in the newborn human infant and the fact that in the 3-week-old infant these elements have undergone "regressive changes." As mentioned previously, I think the presence of these elements in the neocortex of the newborn cat contributes to the

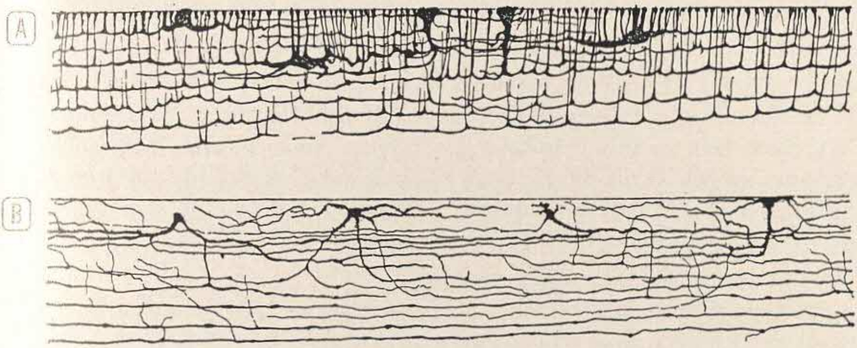

FIGURE 129. (*A*) Horizontal neurons in plexiform layer of visual cortex of a newborn human infant. (*B*) Plexiform layer of visual cortex of 20-day-old infant. Note absence of numerous radially oriented processes of horizontal cells which, in the newborn infant, make contact with the pial surface. Golgi method. Reprinted from Ramón y Cajal, S.: *Histologie du Système Nerveux de l'Homme et des Vertébrés*. Paris, A. Maloine, 1909.

differences in the physiological and pharmacological characteristics of the SCR in the neonatal period. It is well known that the EEG of the newborn cat is very poorly organized and yet axodendritic pathways in the superficial neuropil are fairly well developed. What changes account for the fact that a mature type of EEG is detectable by the 2nd to 3rd post-natal week? I suspect that the expansion of the area for synaptic contacts on cortical neurons brought about by proliferation of the basilar dendritic system and the growth of axon-collaterals represent the major maturational changes in the neocortex.

*Doty:* Spontaneous activity in the hippocampus is at normal level at birth, did you say?

*Purpura:* We can't draw that conclusion, because in our preparations we have recorded from the hippocampus after removing the overlying neocortex. Under these conditions, the hippocampus is undoubtedly somewhat depressed, but the depression does not interfere with the demonstration of post-tetanic facilitation or seizure activity at birth. The important point is that post-tetanic facilitation either of the SCR or of specific thalamocortical evoked responses has not been observed in the newborn cat, although we have some data that nonspecific thalamocortical responses may exhibit post-tetanic facilitation.

*Fremont-Smith:* Do you mean electrical seizure activity?

*Purpura:* The seizure is induced with a pharmacological agent.

*Bodian:* I am glad to hear someone attempt to relate the organization of the neurons in the cortex to physiological activity. I wonder, however, whether one can put complete faith at the present time in your concept of change in the horizontal cells, because it is based purely on the Golgi method, with its possible variation in staining precision from one stage to another. I don't discount the possibility that there may be regression. We have this in other embryonic systems, such as the Rohon-Beard cells in amphibia and similar cells in mammals, apparently, as described by Humphrey (26). But I think, before you go very far in assuming that the horizontal cell regresses, we would want to see a good deal of material, possibly with other methods.

I would like to ask whether incision between the stimulating electrode and the recording one has been attempted? Is it clear in your mind that the horizontal cell is the key to this spread?

*Purpura:* First let me say that I stressed the development of the horizontal cells to illustrate the different varieties of dendritic elements present at birth in the cat. Whether there is a true "regression" of the Cajal-Retzius cells, I certainly can't answer except to say that they are present at birth in the cat and human infant (17,53) as shown by the Golgi method, but the dendritic arborization characteristic of the embryonic cell is not seen in the mature cortex. The spread of the SCR probably involves horizontal axons in the molecular layer, as well as pathways with a more circuitous trajectory involving elements in submolecular regions (49).

*Magoun:* Dr. Windle, would you like to make some closing remarks concerning the first part of the discussion?

*Windle:* I suppose that we are all concerned with behavior, and how to arrive at a full understanding of behavior is the big question. I am confident that we will not, in our lifetime, fully understand behavior. But we are making great progress toward its understanding, and meetings such as these contribute enormously, not by assembling all the facts that are available, but by sampling them.

The meeting so far has provided, in three different areas, samples of certain facts that have a bearing on behavior. I would add a word of caution now. Let us not be precipitous in deciding what it is that makes man behave like man. Let us get more and more facts.

I am impressed more by the lack of knowledge in certain areas than I am by the presence of sufficient facts. I suppose I am more of a neuroembryologist than anything else; and I am appalled at the dearth of new contributions to development of the nervous system in the last 20 or even 30 years. Who today in the United States is making a real effort to study the development of the nervous system, the development of behavior?

I think most of you are aware of the quiet revolution that has been taking place in our knowledge of the structure of the brain. This, to me, is one of the most impressive things that has happened in biomedical science. It has happened within the last 6 years and seems to be moving rapidly today. Our concepts of the nerve cell, neuroglial cell, and other types of cells are changing very rapidly.

All of us must take into consideration the new concepts of neurocytology, chemistry, and physiology in attempting to arrive at an understanding of behavior. I would urge that we go out of our way to try to bring our knowledge up to date in these areas.

One can view behavior and the development of maturation from several points of view. All of us are trying to achieve the same goal, by different means. One great advantage of such meetings as this is to be able to come together occasionally and listen to people from distant lands, whose techniques are different from those with which we are familiar.

## REFERENCES

1. ADRIAN, E. D.: The spread of activity in the cerebral cortex. *J. Physiol.* **88,** *127-161 (1936).*
2. ———: *The Physical Background of Perception.* Oxford, Clarendon Press, 1947.
3. ANOKHIN, P. K.: *Problems of Higher Nervous Activity.* Moscow, Academy of Medical Sciences, USSR., 1949. (In Russian)
4. BAILEY, P., and DAVIS, E. W.: Effects of lesions of periaqueductal gray matter in cat. *Proc. Soc. Exper. Biol. & Med.* **51,** *305-306 (1942).*
5. ———: Effects of lesions of periaqueductal gray matter on *Macaca mulatta. J. Neuropath. & Exper. Neurol.* **3,** *69-72 (1944).*
6. BATSEL, H. L.: EEG patterns of waking in the chronic isolated cerebrum of the dog. *Rep. #380 U. S. Army Med. Res. Lab., Fort Knox, Ky.*, April 1959.
7. ———: Electroencephalographic synchronization and desynchronization in the chronic "cerveau isolé" of the dog. *EEG Clin. Neurophysiol.* **12,** *421-430 (1960).*
8. BECK, E. C., DOTY, R. W., and KOOI, K. A.: Electrocortical reactions associated with conditioned flexion reflexes. *EEG Clin. Neurophysiol.* **10,** *279-289 (1958).*
9. BENOIT, O.: Étude des variations de l'activation corticale provoquée par des stimulations réticulaires en expérience chronique. *J. Physiol. Paris* **50,** *153-155 (1958).*
10. BIRUKOV, G.: Ermüdung und Umstimmung bei Gleichgewichtsreaktionen der Amphibien. Verhandl. deutsch. Zool. Gesellsch. Wilhelmshaven, 1951 (pp. 144-150). *Zoologischer Anzeiger Suppl. 16, 1952.*

11. Bridger, W. H., and Reiser, M. F.: Psychophysiological studies of the neonate: An approach toward the methodological and theoretical problems involved. *Psychosom. Med.* **21**, *265-276 (1959).*
12. Brooks, V. B., and Enger, P. S.: Spread of directly evoked responses in the cat's cerebral cortex. *J. Gen. Physiol.* **42**, *761-777 (1959).*
13. Carmichael, M. W., Housepian, E. M., and Purpura, D. P.: Effects of "convulsant" $\omega$-amino acids during cortical maturation (cat). *Fed. Proc.* **19**, *267 (1960).*
14. Chang, H-T.: Dendritic potential of cortical neurons as produced by direct electrical stimulation of the cerebral cortex. *J. Neurophysiol.* **14**, *1-21 (1951).*
15. ———: Some observations on excitability changes of cortical and subcortical neurons and their possible significance in the process of conditioning. Proc. Internat. Cong. EEG and Higher Nervous Activity, Moscow, 1958. *EEG Clin. Neurophysiol. Suppl. 13. 39-46 (1960).*
16. Clare, M. H., and Bishop, G. H.: Properties of dendrites; apical dendrites of the cat cortex. *EEG Clin. Neurophysiol.* **7**, *85-98 (1955).*
17. Conel, J. L.: *The Postnatal Development of the Human Cerebral Cortex. I. The Cortex of the Newborn.* Cambridge, Mass., Harvard Univ. Press, and London, Oxford Univ. Press, 1939.
18. Dement, W., and Kleitman, N.: Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. *EEG Clin. Neurophysiol.* **9**, *673-690 (1957).*
19. Duffy, E.: The psychological significance of the concept of arousal or activation. *Psychol. Rev.* **64**, *265-275 (1957).*
20. Eccles, J. C.: Interpretation of action potentials evoked in the cerebral cortex. *EEG Clin. Neurophysiol.* **3**, *449-464 (1951).*
21. Eikmanns, K-H: Verhaltensphysiologische Untersuchungen über den Beutefang und das Bewegungssehen der Erdkröte (Bufo bufo L.) *Ztschr. f. Tierpsychol.* **12**, *229-253 (1955).*
22. Fuster, J. M.: Tachistoscopic perception in monkeys. *Fed. Proc.* **16**, *43 (1957).*
23. Galambos, R.: Neural mechanisms in audition. *Laryngoscope* **68**, *388-401 (1958).*
24. Gershuni, G. V.: The reflex responses to external stimuli acting on the sense organs as related to the sensation. *Physiol. Journal USSR* **35**, *5 (1949).* (In Russian)
25. Granit, R.: *Receptors and Sensory Perception.* New Haven, Yale Univ. Press, 1955.
26. Humphrey, T.: Primitive neurons in embryonic human central nervous system. *J. Comp. Neurol.* **81**, *1-45 (1944).*
27. Hunt, W. E., and Goldring, S.: Maturation of evoked response of visual cortex in postnatal rabbit. *EEG Clin. Neurophysiol.* **3**, *465-471 (1951).*
28. Ivanov-Smolensky, A. G.: The study of the action of the components of a complex sound stimulus upon the complete elabo-

ration of differentiation. *The Works of Pavlov's Laboratories.* Vols. I and III, 1928. (In Russian)

29. ———: *The Problem of the Pathophysiology of Higher Nervous Activity.* Moscow, 1949. (In Russian)
30. JACOBSON, J. H., and GESTRING, G. I.: Centrifugal influence upon the electroretinogram. *A.M.A. Arch. Ophthalmol.* **60,** *295-302 (1958).*
31. JOHNSON, E. T.: The character of the B-wave in the human electroretinogram. *A.M.A. Arch. Ophth.* **60,** *565-591 (1958).*
32. JOUVET, M.: Recherches sur les mecanismes neurophysiologiques du sommeil et de l'apprentissage négatif. *Brain Mechanisms and Learning.* Montevideo (In press).
33. JUNG, R.: Coordination of specific and non-specific afferent impulses at single neurons of the visual cortex. In: *Reticular Formation of the Brain.* Boston, Little, Brown, 1958 (pp. 423-434).
34. ———: Excitation, inhibition and coordination of cortical neurones. *Exper. Cell. Res. Suppl. 5, 262-271 (1958).*
35. KOFFKA, K.: *Principles of Gestalt-psychology.* New York, Harcourt, 1935.
36. KONORSKI, J., and SZWEJKOWSKA, G.: Chronic extinction and restoration of conditional reflexes. IV. Dependence of the course of extinction and restoration of conditional reflexes on the "history" of conditioned stimulus. *Acta Biol. Exper.* **16** *(1952).*
37. KUFFLER, S.: Synaptic inhibitory mechanisms. Properties of dendrites and problems of excitation in isolated sensory nerve cells. *Exper. Cell. Res. Suppl. 5, 493-519 (1958).*
38. LINDSLEY, D. B.: The reticular system and perceptual discrimination. In: *Reticular Formation of the Brain.* Boston, Little, Brown, 1958 (pp. 513-534).
39. LISSÁK, K., and GRASTYÁN, E.: Changes in hippocampal activity during conditioning. *EEG Clin. Neurophysiol. Suppl. 13, 271-277 (1960).*
40. MALMO, R. B.: Activation: A neuropsychological dimension. *Psychol. Rev.* **66,** *367-386 (1959).*
41. MORRELL, F.: Lasting changes in synaptic organization produced by continuous neuronal bombardment. *Brain Mechanisms and Learning.* Montevideo (In press).
42. PARAMONOVA, N. P.: On the elaboration of fine differentiations without special reinforcement. (In press). (In Russian)
43. PAVLOV, I. P.: *Twenty Years of Experimental Study of the Higher Nervous Activity of Animals.* Sixth Edition. Moscow and Leningrad, 1938. (In Russian)
44. ———: Studies of the action of the cerebral hemispheres. *Complete Collected Works.* IV. 1947. (In Russian)
45. PETRIE, A.: Some psychological aspects of pain and the relief of suffering. *New York Acad. Sc.* **86,** *13-27 (1960).*
46. POLIAKOV, G. I.: Concerning the place of the reticular formation in the systems of analysers. *Uspiekhi sovremiennoi biologii.* **48,** *N.2 (5) (1959).* (In Russian)

47. PURPURA, D. P.: Nature of electrocortical potentials and synaptic organizations in cerebral and cerebellar cortex. *Internat. Rev. Neurobiol.* **1**, *47-163 (1959)*.
48. ———: Pharmacological action of ω-amino acid drugs on different cortical synaptic organizations. In: *Inhibition in the Nervous System and γ-Aminobutyric Acid*. E. Roberts, Ed. Oxford, Pergamon Press, 1960 (pp. 495-515).
49. PURPURA, D. P., CARMICHAEL, M. W., and HOUSEPIAN, E. M.: Physiological and anatomical development of superficial axodendritic synaptic pathway in immature neocortex. *Exper. Neurol.* (In press).
50. PURPURA, D. P., GIRADO, M., SMITH, T. G., CALLAN, D. A., and GRUNDFEST, H.: Structure-activity determinants of pharmacological effects of amino acids and related compounds on central synapses. *J. Neurochem.* **3**, *238-268 (1959)*.
51. PURPURA, D. P., and GRUNDFEST, H.: Nature of dendritic potentials and synaptic mechanisms in cerebral cortex of cat. *J. Neurophysiol.* **19**, *573-595 (1956)*.
52. ———: Comparative pharmacological analyses of different hippocampal synaptic organizations (cat). *Fed. Proc.* **18**, *123 (1959)*.
53. RAMÓN Y CAJAL, S.: *Histologie du Système Nerveux de l'Homme et des Vertébrés*. Paris, A. Maloine, 1909.
54. RETZLAFF, E.: A mechanism for excitation and inhibition of the Mauthner's cells in teleost: A histological and neurophysiological study. *J. Comp. Neurol.* **107**, *209-225 (1957)*.
55. RETZLAFF, E., and FONTAINE, J.: Reciprocal inhibition as indicated by a differential staining reaction. *Science* **131**, *104-105 (1960)*.
56. ROBERTS, E.: Free amino acids of nervous tissue. Some aspects of metabolism of gamma-aminobutyric acid. *Inhibition in the Nervous System and γ-Aminobutyric Acid*. E. Roberts, Ed. Oxford, Pergamon Press, 1960 (p. 144).
57. ROGER, A., VORONIN, L. G., and SOKOLOV, E. N.: An electroencephalographic investigation of the temporary connexion during extinction of the orientation reflex in man. *Pavlov J. Higher Nerv. Act.* **8**, *1-13 (1958)*. (Pagination of English translation)
58. ROWLAND, V.: Differential electroencephalographic response to conditioned auditory stimuli in arousal from sleep. *EEG Clin. Neurophysiol.* **9**, *585-594 (1957)*.
59. SCHERRER, J., and OECONOMOS, D.: Résponses évoquées corticales somesthésiques des mammifères adultes et nouveau-nés. In: *Les Grandes Activités du Lobe Temporale*. T. Alajouanine, Ed. Paris, Masson, 1955 (pp. 249-268).
60. SEGUNDO, J. P., ROIG, J. A., and SOMMER-SMITH, J. A.: Conditioning of reticular formation stimulation effects. *EEG Clin. Neurophysiol.* **11**, *471-484 (1959)*.
61. SERRA, C., PARIANTE, F., and VENTRA, F.: Effetti biologici della stimolazione luminosa intermittente. *Acta neurol.* **11**, *411-425 (1956)*.

62. SHARPLESS, S., and JASPER, H.: Habituation of the arousal reaction. *Brain* **79**, *655-680 (1956)*.
63. SHERRINGTON, C. S.: *Integrative Action of the Nervous System.* New Haven, Yale Univ. Press, 2nd Ed. 1947.
64. SHKOLKIN-IARROS, E. G.: Efferent paths from the visual cortex. *Pavlov J. Higher Nerv. Act.* **1**, *114-128 (1958)*. (Pagination of English translation)
65. SHOLL, D. A.: *The Organization of the Cerebral Cortex.* London, Methuen, and New York, John Wiley & Sons, 1956.
66. SOKOLOV, E. N.: Higher nervous activity and the problem of perception. In: *Proc. XIV Internat. Congr. Psychol.* (Montreal) Amsterdam, North-Holland Pub. Co., 1955 (pp. 134-135).
67. ———: *Perception and Conditional Reflexes.* Moscow Univ., 1958. (In Russian)
68. ———: Neuronal model of the stimulus: 1: The formation of a neuronal model by repeated representation of the stimulus. *Rep. Acad. Pedagog. Sc. USSR* 4 *(1959)*. (In Russian)
69. SOKOLOV, E. N.: The peculiarities of the orienting reflex during the development of sleep inhibition in man. *The Theses of the 9th All-Union Congress of Physiology, Biochemistry, and Pharmacology*, 1959. Vol. I, Moscow-Minsk, 1959. (In Russian)
70. SOKOLOV, E. N., and MIKHALEVSKAYA, M. B.: A study of the properties of threshold responses to signal light stimuli. *Voprosy psychologii.* **3**, *78-90 (1959)*. (In Russian)
71. STEKLOVA, R. P.: Concerning the change of light sensitivity of the eye by action of auditory stimuli of different intensities. *The Orienting Reflex and Problems of Higher Nervous Activity.* Moscow, 1959. (In Russian)
72. SZWEJKOWSKA, G.: The effect of a primary inhibitory stimulus upon the positive salivary conditioned reflex. *Bull. Acad. Polonaise Sc. et Lettres* **5**, *393-396 (1957)*.
73. TISSOT, R., and MONNIER, M.: Dualité du système thalamique de projection diffuse. *EEG Clin. Neurophysiol.* **11**, *675-686 (1959)*.
74. TUNTURI, A. R.: Analysis of cortical auditory responses with probability pulse. *Am. J. Physiol.* **181**, *630-638 (1955)*.
75. ———: Masking of cortical responses in middle ectosylvian auditory area of dog. *Am. J. Physiol.* **184**, *321-328 (1956)*.
76. VINOGRADOVA, O. S.: Concerning the dynamics of the orienting reflex in the process of the elaboration of the conditioned connection. *The Orienting Reflex and Exploratory Behavior*, Moscow, 1958. (In Russian)
77. VINOGRADOVA, O. S., and SOKOLOV, E. N.: The relation of vascular responses in the hand and in the head in some unconditioned reflexes in man. *Sechenov Physiol. Journal USSR* 42, *1, 1957*.
78. VORONIN, L. G.: *Analysis and Synthesis of Compound Stimuli in Normal Dogs and in Dogs with Impaired Hemispheres.* 1948. Moscow Univ. (In Russian)
79. ———: *The Comparative Physiology of Higher Nervous Activity.* Moscow Univ., 1957. (In Russian)

80. VORONIN, L. G., and SOKOLOV, E. N.: Cortical mechanisms of the orienting reflex and their relation to the conditional reflex. Proc. Internat. Conf. on EEG and Higher Nervous Activity. *EEG. Clin. Neurophysiol. Suppl. 13, 335-344 (1960).*
81. WAN TSIN: The neuronal model of the stimulus: II: The neuronal model of the orienting reflex to light. *Rep. Acad. Pedagog. Sc. USSR* 5, *(1959).* (In Russian)
82. WEDENSKY, N. Y.: Concerning a new singular condition of nerve centers produced by prolonged irritation of a sensory nerve. *Sobr. soch.* 4, *150 (1938).* (A Leningrad Univ. Publication) (In Russian).
83. YERKES, R. M.: Inhibition and reinforcement of reaction in the frog *Rana clamitans. J. Comp. Neurol. Psychol.* 14, *124-137 (1904).*

# CONCEPTS OF DRIVE

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I SHALL DISCUSS a piece of work in which I at first tried to use concepts like drive and inhibition and habituation. However, as the work progresses, I find that these concepts are gradually losing their usefulness.

This study is concerned with an analysis of the changes in strength of a response when the only operation performed by the experimenter is to present a stimulus and then to take it away after a certain interval, irrespective of the behavior of the animal. The response is the so-called "mobbing" response of the chaffinch. The chaffinch is a passerine bird, and it gives this response to a wide variety of predators—owls, stoats, snakes, and so on. While mobbing, it calls with a chink-chink call, and it is that which I measure, by counting the number of calls per unit time. Some of these experiments are published (9,10). Others are in progress.

*Fremont-Smith:* Can an isolated bird make the mobbing response, or does it require a mob of birds?

*Hinde:* In nature, the response is made by a mob of birds, but in my experiments, I test them one at a time.

*Fremont-Smith:* And they will give the same response in isolation?

*Hinde:* Yes, so far as I can see, the response is identical. I should say that it is an ambivalent response, in the sense that the animal is in an approach-avoidance conflict while making it.

*Doty:* This is an unlearned response?

*Hinde:* This is a response which is made by birds that have never seen a predator before. It appears about 3 weeks after hatching; that is, just a few days after the birds leave the nest. The bird approaches the predator until it is about 12 feet away.

*Fremont-Smith:* Is it flying?

*Hinde:* Sometimes, but more usually hopping from twig to twig. It swings its body from side to side in intention movements of approaching or moving further away. At the same time, it makes these chink-chink calls. Nearly all the time it is edging a little bit nearer or a little bit farther away. However, the only aspect which I shall talk about today is these chink-chink calls.

Some examples of the way in which the rate of calling changes with time are shown in Figure 130. The response first rises to a peak, which usually comes in the first 2 or 3 minutes, and then it falls gradually away.

*Brazier:* The "predator" is a stuffed owl?

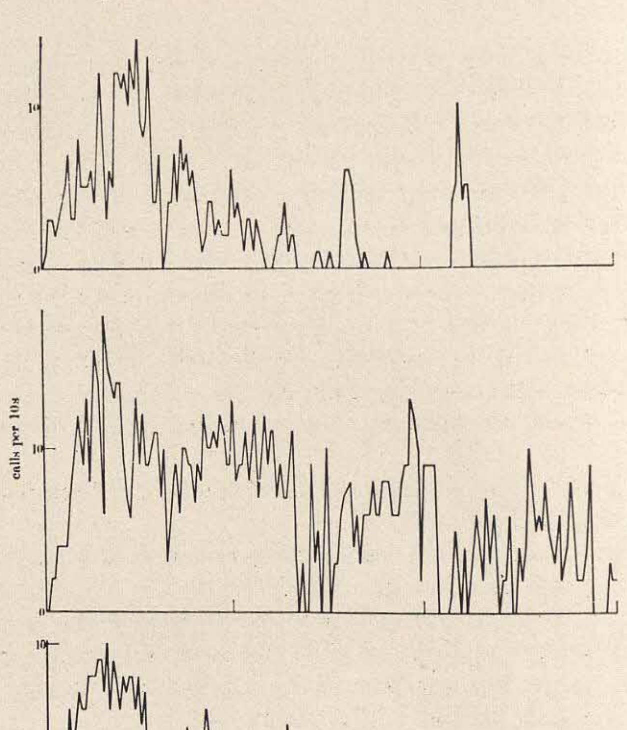

FIGURE 130. Some examples of the course of the owl-mobbing response. Ordinate = calls per 10-second period. Abscissa = interval, in minutes, since presentation of stimulus. Reprinted, by permission, from Hinde, R. A.: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaffinch (*Fringilla coelebs*). I. The nature of the response, and an examination of its course. *Proc. Roy. Soc. London B.* 142, *306-331 (1954).*

*Hinde:* Yes, a stuffed owl. I have done it with live owls as well, and I will discuss that presently.

*Fremont-Smith:* This is the habituation of an orienting reflex?

*Hinde:* That is what I want to discuss. The measure that I have used mostly has been the number of calls given in the first 6 minutes of a presentation. If two successive presentations are made, with a rest interval in between, the ratio of the number of calls given in the first 6 minutes of the second presentation to the number given in the first 6 minutes of the first presentation gives an index of the recovery during the rest interval.

Figure 131 expresses this as percentages and shows a recovery curve after a 30-minute initial presentation of an owl. After short rest intervals, the response is much reduced, but it recovers to 50 per cent after 30 minutes or so. There is little further recovery in 24 hours, and even in the next few days.

In the experiments that I shall discuss at this time, I used two stimuli —a stuffed owl and a toy dog. These look very different from each other; one is brown and the other is white, and they are a different shape and texture, and so on. My aim was to try to analyze the processes underlying these changes in the strength of the response by

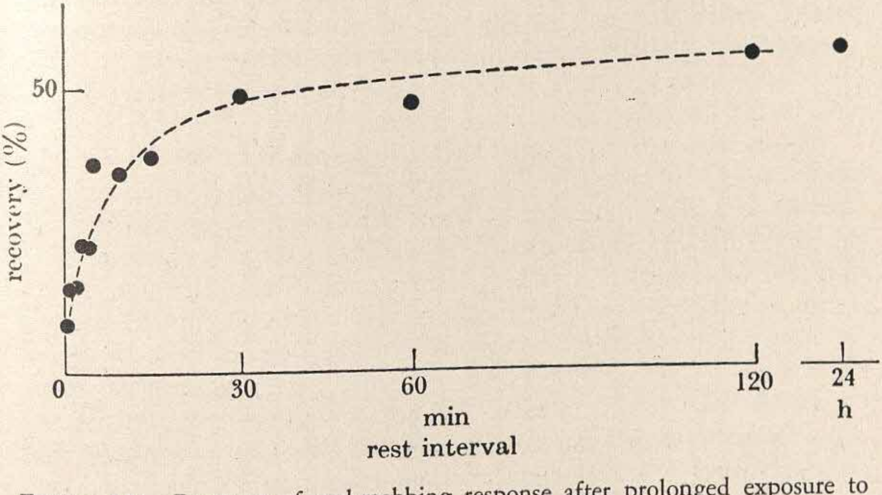

FIGURE 131. Recovery of owl-mobbing response after prolonged exposure to stuffed Tawny Owl. Reprinted, by permission, from Hinde, R. A.: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaffinch (*Fringilla coelebs*). II. The waning of the response. *Proc. Roy. Soc. London B.* 142, *306-331 (1954).*

varying the length of the initial presentation, the length of the rest interval, and the strength of the stimulus.

The chaffinches used were caught wild, each individual having been kept for a short while after trapping, then subjected to one series of presentations, marked, and released. Of the two stimuli, the owl is a stronger stimulus than the dog. It is convenient to use the log of the number of calls given in the first 6 minutes as an index of response strength: naive birds gave a mean of 2.21 to the owl and 1.91 to the dog.

In addition to the number of calls given in the first 6 minutes, various other parameters were measured—the latency to the first call, the minute in which the peak rate of calling occurred, and the rate at which the response waned as indicated by the ratio of the logarithm of the number of calls given in the second 6 minutes to the number given in the first 6 minutes. The correlations between these various characteristics of the response are not high, indicating a considerable degree of complexity in the underlying mechanisms. In responses to the dog, the latency is longer, the peak minute comes earlier, and the response wanes more rapidly than in responses to the owl. The relationships of the logarithm of the number of calls given in the first 6 minutes to the rate at which the response wanes is similar for both the stimuli. In other words, the rate at which the response wanes depends on response strength rather than on stimulus strength. In most of the experiments which follow, I shall be concerned primarily with the number of calls given in the first 6 minutes; analysis of the changes in the other parameters is still incomplete.

The first series of results that I want to discuss is concerned with the long-term effects of a stimulus presentation; that is, I presented one stimulus and then waited for 24 hours before presenting the next one. Figure 132 shows the results of an earlier series of experiments, to illustrate the extent of this long-term waning effect. In these experiments, an owl was presented for 20 minutes once a day for 12 successive days. The response, as measured by the number of calls given, diminished to less than 10 per cent of its initial strength. This happened even when a live owl was used. In another series of experiments, not shown in this graph, I put in a live owl for 6 minutes a day, and after each presentation, I went into the aviary, caught the chaffinch, and held it in my hand against the owl's breast while I pulled out two of the chaffinch's feathers, and still the habituation occurred.

Figure 133 shows the results of a series of experiments in which the stimulus sequences owl-owl, dog-dog, dog-owl, and owl-dog were pre-

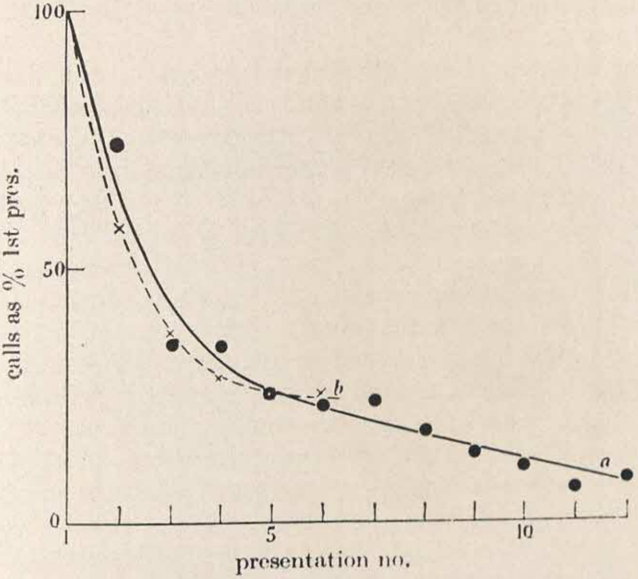

FIGURE 132. Habituation curves. Continuous line = to live Little Owl presented for 20 minutes a day in aviaries. Broken line = to stuffed Tawny Owl for 3 minutes a day in cages. Strength of response plotted as percentage of calls given in first presentation averaged for all individuals for each presentation. Reprinted, by permission, from Hinde, R. A.: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaffinch (*Fringilla coelebs*). II. The waning of the response. *Proc. Roy. Soc. London B.* 142, *331-358 (1954).*

sented. In each case, the rest interval between presentations was 24 hours, so we are dealing here with the long-term effects of the initial presentation. The length of the initial presentation was varied: 12 minutes, 24 minutes, 48 minutes, or 24 hours. Birds were distributed between groups in such a manner that the mean response strength to dog or to owl on first presentation was closely similar to that of the population as a whole. Figure 133 shows the relation between the strength of the response on the second presentation and the length of the first presentation.

In nearly all these experiments, the mean response strength on the second presentation was smaller than that which the same stimulus produced from naive birds; in other words, there was a decrease in response strength even when there had been a radical change in the stimulus. This was not true of some of the owl-dog combinations, which I shall mention presently.

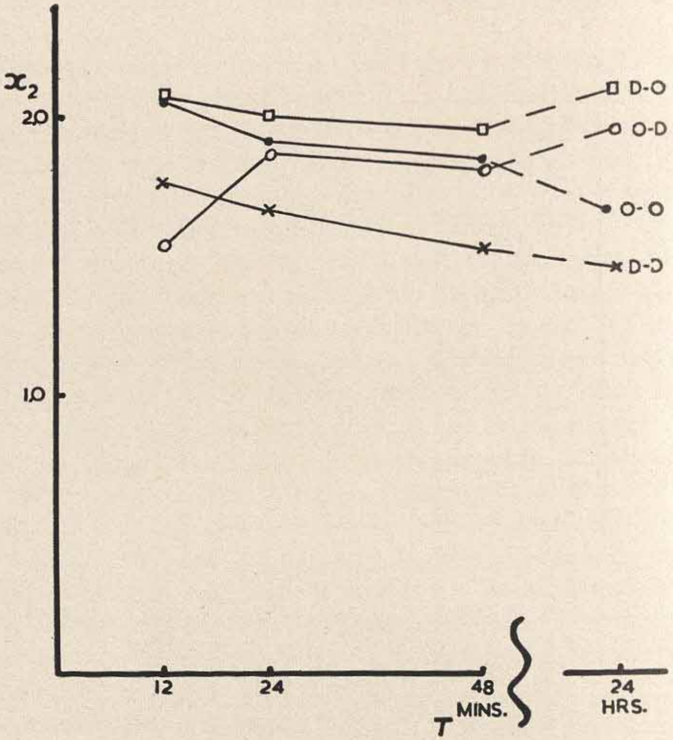

FIGURE 133. Effect of varying the length of the initial presentation on the response strength after a 24-hour rest interval. Ordinate = logarithm of number of calls in first 6 minutes of second presentation. Abscissa = length of initial presentation. D = dog; O = owl.

When the same stimulus was repeated, that is, with owl-owl and with dog-dog, increasing the length of the initial presentation caused a decrease in the response on the second occasion. With dog-owl, increasing the length of the initial presentation made no significant difference to the second response. With owl-dog, increasing the length of the initial presentation of owl caused a gradual increase in the subsequent response to dog; with long initial presentations of the owl, the response to dog was higher than it would have been if the chaffinch had not seen the owl.

*Brazier:* May I ask if it makes any difference how you orient your stuffed owl? Supposing you present it first in the vertical position, and then prone with its face hidden, does this make any difference?

*Hinde:* It makes some difference, but very little; the difference there is, of course, much less than the difference between a dog and an owl.

*Leake:* But you always present the face forward?

*Hinde:* Yes.

*Purpura:* Does it make any difference if the wings are spread?

*Hinde:* I don't think it does. Hartley (8) has done some experiments on this, but I don't know exactly what results he got on this point, The most important character of an owl is the eyes, which I shall mention in a moment.

The second point here is that with those combinations in which the owl was shown second, the second response was uniformly greater when dog was shown first than when owl was shown first. In other words, the habituation is to some extent specific to the stimulus. When you look at the combinations in which dog was shown second, this is true with a 12-minute initial presentation, but with longer initial presentations, the response is greater after owl than it is after the dog.

This suggests a long-term positive effect as well as a long-term negative one, and I think that what one is measuring here is a result of two effects, one leading to an increase in response strength and the other leading to a decrease.

In these experiments, the positive effect was just sufficient in the owl-dog series to cause the response to dog to be greater than it would have been without the initial presentation. In an earlier series of experiments, a similar phenomenon was shown rather more dramatically. Here, the stimuli used were two flat wooden models, painted in owl colors and similar except that one had representations of eyes and the other did not. Model C, which had eyes, elicited from naive birds about four times as many calls in the first 6 minutes as did Model D, which had no eyes. When birds were shown Model D for 20 minutes on one day and then Model C on the next, the response to Model C was much reduced as compared with the response of naive birds. However, when Model C was shown first, the average response to Model D on the next day was double that of naive birds. Thus, in this experiment, the resultant was in one case an increase in response strength and in the other a decrease. This positive effect is also shown by a decrease in the latency of the response, but I think I won't go into that now.

*Leake:* How wide a variation occurs in those mean figures?

*Hinde:* All the differences which I have mentioned are significant at $P<0.05$ or better.

*Windle:* Can you cover all of the owl except the eyes, something like the Cheshire cat in "Alice in Wonderland," and still get a response? Is the eye the necessary thing?

*Hinde:* It's certainly one of the most important characters of the stimulus. This response of small birds to owls' eyes has also been demonstrated in *Lepidoptera.* The eyes on the wings of butterflies and moths are often near-perfect representations of owls' eyes and are fear-provoking stimuli, which are shown off to potential predators. The predator in that case is a chaffinch or a bird like it, and it may be deterred by the display. This is work of Blest (2) at Oxford.

*Sokolov:* Are the eyes of the owl effective only against the background of the shape of the owl? Or are points as symbols of eyes equally effective?

*Hinde:* If two pieces of wood are presented, one with eyes and the other without, the former is the more effective.

*Fremont-Smith:* Suppose you use eyes alone, with no square, no circle, or anything else?

*Hinde:* The nearest I can get to that are the butterflies.

*Fremont-Smith:* But you could put eyes on a very thin stick, couldn't you?

*Hinde:* In reply, I can quote one of Blest's (2) experiments. He was interested, really, in the response of passerine birds to eye spots on the wings of butterflies and moths. He had a small box with two ground glass screens on the top, each screen having a light beneath it. He could put a slide beneath the screens in such a manner that the pattern on the slide appeared on the screen. He put a mealworm or some such creature in the middle, and when the bird settled on the box to pick up the mealworm, he pressed a switch and the patterns appeared on the screens. He could thereby test the effectiveness of various patterns, and he found that circles were much more effective than crosses of similar area, and so on, and that the more the pattern was like a vertebrate eye, the more effective it was.

*Fremont-Smith:* This is somewhat analogous to Tinbergen's experiments with gulls' beaks.

*Hinde:* Yes, he was a student of Tinbergen's.

*Leese:* Dr. Hinde, on the specificity of stimulus, I've been wondering about what I might call phylogenetic motivation. You spoke of the apparent specificity of the two circles suggestive of the two eyes. That may be a peak stimulus. How about comparing that with one circle or three circles or four circles, where there is a possible difference in peak specificity of the stimulus?

*Hinde:* This could be done. The only experiments that approach that, that I know about, are those of Blest (2), and he was interested in a specific problem; that is, his work arose out of the problem of why moths have these eye spots, and he tested patterns comparable to those that moths have. But I agree this could be done.

*Reynolds:* Birds of prey, also, are quite obsessed with eyes, the counterpart of the small bird reaction. In the case of the accipitrine hawks, which are the short-range attack hawks, represented in the United States by the goshawk, the Cooper's hawk, and the sharp-shinned hawk, the response to identifying prey is to turn the head away from it; in other words, to hide the eyes. They will sometimes bring the wing up, also, in order to double the screen between themselves and the prey, and they will actually start to attack with the head turned in the opposite direction. I think it would be very hard to visualize this as an avoidance response; yet, it is turning away from the place they intend to go.

*Fremont-Smith:* This is after identification?

*Reynolds:* Yes. They will look at the prey first, and then bob the head. I don't know whether this is a range-finding maneuver or whether it has some other basis such as to shield itself from the prey, but as soon as an Accipiter identifies an object as prey, it turns its head, raises its wing, and then hurls itself at the prey. From then on, it will take advantage of any cover that is available, so as to hide its eyes. At least, I am assuming, it is its eyes.

The trained falcon that you bring to your hand will do the same thing. He will fly in such a fashion that his eyes are hidden from your eyes by your arm, and his eyes will not meet yours until he has hit the food that you are holding in your hand. Then, he will swing up, stare you in the eyes, and start to eat.

This applies to the Accipiters. The other more long-range attack hawks don't do this. But something similar applies to other birds of prey, in that all of these birds seem to identify people by their faces, and it appears that this is identification by the eyes, because if one wears a mask or even eyeglasses, they are likely not to identify the person with whom they are oriented.

Furthermore, there are two species of birds that have been repeated mankillers, the great horned owl and the great blue heron, and both of these birds kill by attacking the eyes.

*Hinde:* The long-term habituation is due to different processes from the short-term waning effects. Figure 131 showed that recovery takes place during the first 30 minutes but then approaches an asymptote. This suggests that there are short-term processes from which recovery occurs, and also more permanent learning effects. This view is confirmed by the observation that other characteristics of the second response change with increase in length of the rest interval. In particular, the slope of the regression line relating the logarithm of the number of calls given in the first 6 minutes to the rate of waning is steeper for second responses after short rest intervals than for experimentally naive birds. As the rest interval increases, the slope decreases, and the regression line for birds tested after a 24-hour rest interval does not differ from that obtained from naive birds.

*Fremont-Smith:* Dr. Hinde, to bring this back to man, would you like to comment on the role of the eyes when a human face mask was presented to infants in experiments carried out at the Tavistock Clinic?

*Hinde:* Yes, Ahrens (1) found that, with a very young baby who was just beginning to smile, the best stimulus for evoking smiling was a white mask with two black spots on it. He also found that all other features, such as eyebrows and noses and mouths, just decreased the response.

In the next series of my experiments on short-term effects, the initial presentation was kept constant at 12 minutes, and the rest interval varied—½, 2½, and 5 minutes, and 24 hours. The same four combinations of stimuli were used as before. The results are summarized in Figure 134. With each combination, there is a tendency for the response on the second presentation to increase with increasing rest interval, as would be expected. This is a manifestation of one or more short-term processes, leading to a decrease in response strength, which dissipate with time.

With the dog-dog combination, the response at ½ minute was significantly greater than the response at 2½ minutes. The recovery curve is thus not a smooth one. Similarly, with owl-dog, the response after 2½ minutes is greater than after ½ minute or after 5 minutes, though these differences are barely significant.

*Bodian:* Were these paradoxical responses associated with any ambivalence of movement? Were the birds more ambivalent in approaching and retreating when they gave this paradoxical number of calls?

*Hinde:* Not to my knowledge.

*Fremont-Smith:* They were always somewhat ambivalent, weren't they? This is part of the process itself.

*Hinde:* Yes. With these short rest intervals, the decremental effect is again to some extent specific to the stimulus used. For instance, when dog is shown on second presentation, the reduction in the response is greater when dog was shown first than when owl was shown first at short rest intervals, but at longer rest intervals the reverse is the case. Similarly, at ½ minute, the response to owl is less if owl was shown

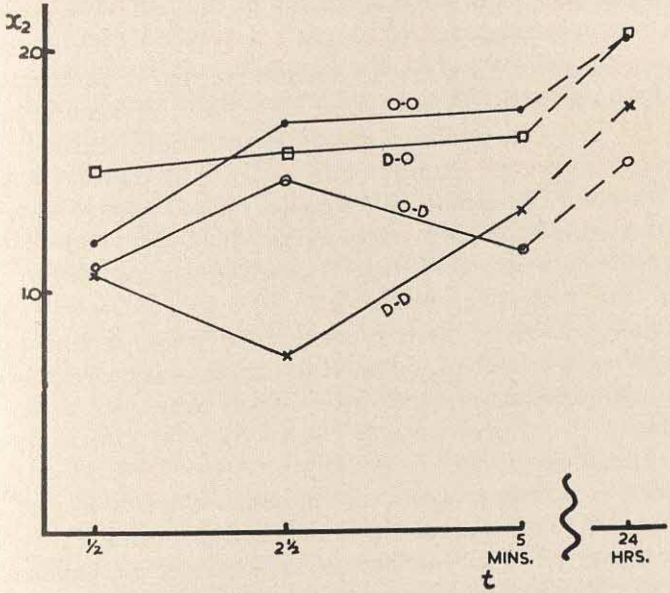

FIGURE 134. Effect of a 12-minute initial presentation on the response strength after a variable rest interval. Ordinate = logarithm of number of calls in first 6 minutes of second presentation. Abscissa = length of rest interval; D = dog; O = owl.

first than if dog was shown first, but with longer intervals this is reversed.

The anomalous points (½-minute rest interval in the dog-dog series and 2½ minutes in the owl-dog series) cannot be dismissed as merely due to sampling errors. One possibility is that we are actually dealing with two short-term processes—one leading to an increase in response strength but decaying rapidly, and the other leading to a decrease in response strength, accumulating and decaying more slowly than the first. If these interacted in a multiplicative fashion, they could well produce a recovery curve with a kink in it.

Of course, practically anything can be explained by summing curves, and the justification for this view must depend on further experiments in which one of the supposed processes is influenced differentially from the other, to produce predictable changes in the recovery curve. Some support is derived from experiments using dog-dog and owl-dog sequences in which the initial presentation was only 2 minutes in length. With such a short initial presentation, we might expect the negative effect to be small, and the positive one to be more clearly revealed. A comparison between the first minute of the second presentation and the second minute of the first presentation reveals whether the resultant response strength increased or decreased during the rest interval. With very short rest intervals (3 seconds or ½ minute), the number of calls given in the first minute of the second presentation is usually smaller than the number in the second minute of the first presentation. With longer intervals (2½ minutes or 5 minutes) it is greater, and with very long intervals (24 hours) it is once again smaller. This experiment thus supports the suggestion that there is one or more short-term positive effects as well as negative ones.

Thus, we now have long-term effects (decaying over days and weeks), both positive and negative, and short-term effects (decaying over minutes), also both positive and negative. Next, I would like to say a word or two about the very short-term effects, decaying over a period of seconds.

The calls, as I mentioned, come in phrases, "chink-chink" or "chink-chink-chink," usually up to about five calls in each phrase. This suggests that when one call is given, there is an increased probability that a second call will be given immediately afterward, and that there is a more gradually accumulating inhibitory effect which is instrumental in causing the end of the phrases.

*Fremont-Smith:* Have you tried two or three birds at a time to see whether the sound of other birds might have caused it to go on longer or stop?

*Hinde:* I have done something rather similar to that, which I am just coming to. I want to take up this question of the very short-term effects, not with the mobbing response, but with the singing of chaffinches, because this lends itself to this purpose rather better.

By using various techniques, Thorpe (18) has been able to teach chaffinches, which have been kept isolated from other chaffinches, strange songs. He used a song tutor, which plays a song every so many seconds while the birds are shut up in a soundproof room. A chaffinch which has two or more songs in its repertoire sings in bouts of one song type, followed by a gap, and then it changes over to another song type. Each bout may comprise something like ten songs, and the interval between successive similar songs in a bout is on the average considerably smaller than the intervals between bouts, during which there is a change of song type.

Song-song intervals are never less than 3 seconds, so it must be assumed that there is some sort of inhibitory effect which depresses the probability of another song being given immediately after one has just been sung. Whether this inhibitory effect is due to something inside the nervous system or outside I am, of course, not able to say.

*Leake:* Could it be assumed that it is fatigue?

*Hinde:* "Fatigue" is a sort of descriptive word that covers all of these factors. Do you mean muscular fatigue?

*Leake:* No, central nervous system fatigue.

*Hinde:* I would regard central nervous system fatigue as being the whole problem I am trying to analyze. Even though this inhibitory effect influenced both song types equally, the mechanism of the change-over from one song type to the other would still remain unexplained. On the other hand, if it affected especially the song type just uttered, a change would be expected from one song type to the other more often than on a random distribution, rather than less often. And so, I think it must be assumed that there is a positive effect, a persisting tendency to repeat the song just uttered rather than another song type. This is probably a consequence of performance, and a further experiment suggests that it may be a consequence of the bird's having just heard itself sing that song type. In this experiment, I played back to chaffinches recordings of their own songs, to see whether this influenced their rate of singing and whether it influenced the proportion of the song type being played in the songs they produced. The results showed that hearing a particular song type causes an increase in the proportion of that song type which is produced. This is probably of adaptive significance, since in nature these birds sing against each other across territorial boundaries (11).

Here again there seem to be conflicting positive and negative effects consequent to the performance, but this time they decay over a period of seconds. The time constants of the very short-term processes in the mobbing response are not the same as those in singing, but they are of the same order.

Going back to the mobbing response for a moment, Figure 135 shows the average number of calls per phrase in successive minutes of a mobbing response, plotted against the total number of calls given in that minute. As would be expected, the greater the total number of calls, the longer the phrases tend to be. But the first 3 minutes of the presentation are numbered, and it is evident that the phrase length during this warming-up period is shorter than would be expected from the rest of the presentation. In other words, the relationship between these very short-term positive and negative effects changes during the course of the warming-up period.

The sort of conclusions that I would like to draw from these experi-

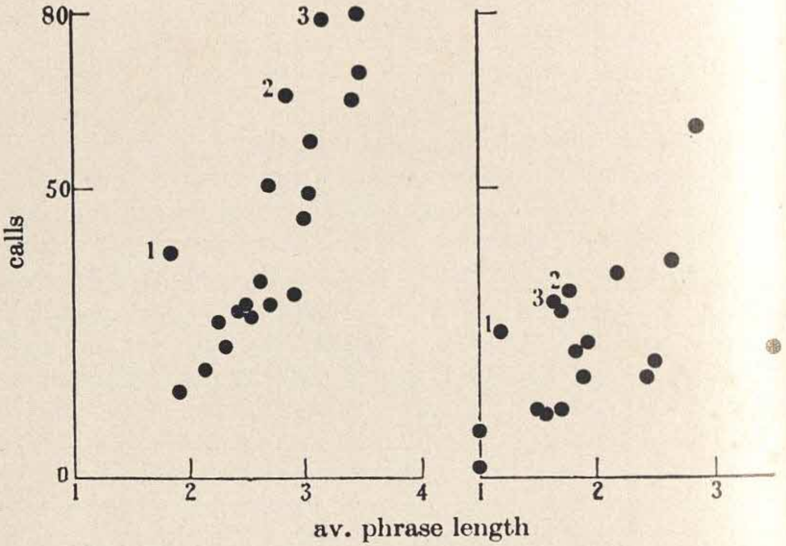

FIGURE 135. Relation between average phrase length and rate of calling for two chaffinches. The records for the first 3 minutes of each presentation are numbered. Ordinate = number of calls per minute. Abscissa = average phrase length in each minute. Reprinted, by permission, from Hinde, R. A.: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaffinch (*Fringilla coelebs*). I. The nature of the response, and an examination of its course. *Proc. Roy. Soc. London B.* 142, *306-331 (1954).*

ments, which are still very much in progress, are these: first, every response or every stimulus presentation causes a change in the animal which affects subsequent responses. Second, this waning or fatigue, or whatever it is to be called, is not a unitary process, but probably depends on a number of quite different processes going on inside the animal. I don't think that it can be explained in terms of spread of inhibition or any other unitary function of that sort. Third, long-term habituation is inextricably interwoven with conditioning, and is not simple. The response decrement which one measures in an habituation experiment may be the result of two effects, positive and negative. Perhaps the same is true of the response increment measured in a conditioning experiment. Fourth, habituation is not independent of the experimental situation, and the degree of generalization probably depends on constant features of the environment. I am suggesting here that the presentation of a dog, for example, causes a subsequent decrease in the responsiveness to a different stimulus 24 hours later, in part because the experimental situation is constant, and what one is presenting is dog-in-the-circumstances-of-the-experiment. I should say, perhaps, that nothing happened to the birds in these experiments in between the presentation of one stimulus and the presentation of the next. They were visually isolated and, as it were, just waiting for the next experiment to happen.

Next, in any work of this sort, which involves successive presentations of stimuli, the time interval between tests may be very highly critical. Indeed, the effect of changing the time interval cannot be predicted with any certainty. Thus, the generalization which Dr. Bridger made earlier in saying that the decrement was increased by increasing the length of the presentation or by decreasing the length of the rest intervals is not necessarily always valid.

Both positive and negative learning are proceeding simultaneously, and if you hold to the view that a change in motivation goes with learning, what sort of motivational model are you going to make for this?

*Fremont-Smith:* There are the experiments by Erich von Holst,* on birds, that provide the possibility of conflicting motivations going on at one time. He implanted two electrodes by which he stimulated the escaping tendency and the brooding tendency simultaneously. Do you know the experiments?

*Hinde:* Yes. In that case, there are two different types of behavior, but here there is only one type.

*Harlow:* Are you measuring one type of behavior or one type of response while two types of behavior are going on? You are only measuring the sound. You said that the animals were approaching and retreating?

*Hinde:* We have begun an analysis of the relationship of the call to approaching and retreating. It looks as though the call is associated with flying, but associated equally with flying in both directions.

*Leake:* There is no correlation, then, between the call and either retreating or approaching?

*Hinde:* Not as far as we can see at the moment.

*Harlow:* Then, the counts of the call represent a resultant of the approaching and retreating?

*Hinde:* Yes, that is what it looks like.

*Leake:* Do I understand that you feel there is no justification for linking the use of a concept of unitary drive with the notion of a center localized in the central nervous system?

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*Personal communication.

*Hinde:* I think that is a big issue.

*Leake:* You asked the question, in fact.

*Hinde:* I think that the first difficulty is that the term *drive* is used to explain many different phenomena which don't necessarily have the same underlying causal mechanism. For example, it is used to explain changes in response strength; to explain apparent spontaneity; to explain the persisting effects of a stimulus, as when people say that the stimulus arouses the drive, which then persists until the next stimulus is given; to explain the persistence of a response (the after-response is often ascribed to the continued presence of a drive); to explain the association in time of functionally related activities, so that when an animal is seen gathering nest material, carrying it, and placing it in the nest, it might be said that these are all associated in time because they are all activated by a nest-building drive. The concept of drive is used also to explain the occurrence of learning, and so on.

These are all quite different phenomena, and therefore, before talking about a unitary drive, it is necessary to know or decide just which of these phenomena one is trying to explain. Then, if the decision is to limit the questions and focus interest on explaining changes in response strength, the question might then be legitimately asked, "Is this drive localized in a place in the nervous system?" I think that an examination of the ways in which the different factors which influence response strength act shows that it is impossible to do this.

For instance, the administration of hormones may influence effectors, feedback from effectors, secondary sexual characters, the production of other hormones, a part of the hypothalamus, or the reticular system, and so on. One hormone may influence response strength by acting in more than one place, and it becomes, as far as I can see, rather meaningless to look for any one place where all these factors are added together (12).

*Bodian:* Speaking as an outsider, do I understand this total situation as being an attempt to study drive by means of an analysis of stimulus and response? So far, I am uncomfortable about your measurements. You found a good measure of response—the call. I am unclear about what the call says about discrimination of various components of the stimulus. Does the ambivalence contain possible components of recognition, as distinct from anxiety about the various elements of the stimulus, so that the response may be excessively complex? Isn't this going to make it rather difficult to pull out of it any concepts of drive?

*Hinde:* One of my points is that a drive concept doesn't help very much in understanding these changes in response strength.

*Bodian:* I'm putting this in the worst possible way, because of my confusion about the kind of data you are presenting.

*Hinde:* I can't say that I really follow you, but, if I may make one point first, perhaps this will help us to get into communication. You talked about all the different stimuli or stimulus elements present, but here both the approach and the avoidance are caused by the same stimulus characters.

*Bodian:* But you gave a few models, the model of the owl with the eyes and without the eyes, in which various components of the stimulus might be producing rather different responses. Curiosity, if you will, might further produce an approach. Anxiety produces an approach as well as a retreat. The only response that seems relatively pure is the retreat. Maybe it isn't, but it seems to me that it might be a little cleaner than the approach.

*Fremont-Smith:* What about aggression?

*Bodian:* Yes, there is aggression, too, with the anxiety, and there is curiosity as distinct from these.

*Hinde:* I think that these lie on a quantitative scale. You mention curiosity. If an owl is shown a young chaffinch in which the owl-mobbing response has not yet fully matured, the chaffinch shows curiosity toward the owl. If a model which is very weak in owl stimulus characters is shown to an adult chaffinch, the chaffinch shows curiosity; it approaches the model and peers at it. Thus, curiosity is something which lies at one end of this scale, apparently, and which appears most conspicuously when either the internal or external factors are low.

Can we just come back to this question that Dr. Bodian raised? Do I understand that the difficulty is that with such a complicated stimulus as an owl or a dog you feel that the two different aspects of approach and avoidance must be caused by different stimulus elements?

*Bodian:* I raised that possibility. I gathered that there might be an idea that the ambivalence is a unitary response, and, if that is the case, perhaps it is a simpler stimulus than I had visualized. But, really, what I would most like to have clarified is that the response you are measuring is not being disturbed by the complexity of the stimulus, that it has a relationship to the strength of the stimulus. If it is only a resultant of various components of the stimulus, the analysis would be very difficult.

For example, when Dr. Leake asked about the variation, you said that the significance was $P<0.05$. But that doesn't tell us what the scatter is. Is it a large scatter?

*Hinde:* Yes, it is a large scatter.

*Bodian:* I think that this raises the possibility that it is a rather shaky response to be measuring.

*Hinde:* This is a difficulty that we constantly meet in starting with a natural or seminatural situation and trying to take it into experimental conditions. We are asked, "Why don't you work with simpler stimuli?" The answer always is that these types of behavior can't be evoked with simpler stimuli.

I would like to give one case where an ambivalent response can be evoked by a relatively simple stimulus, and where I think your sort of problem would be less valid. That is in the threat responses of birds. There is a good deal of evidence that when a bird shows a posture which we functionally call a "threat posture," because it has an intimidating effect on other individuals, the bird is itself in a conflict situation between attacking and fleeing. One type of evidence is from the behavior of two birds in neighboring territories; when the territory owner sees an intruder, he will attack it, and if he is caught off his own territory by another bird, he will flee. But on the boundary, and only on the boundary, these threat postures are adopted.

Lack (13) studied this fighting behavior in the robin, not the American robin but the European one, which has a really red breast. He tried to investigate the stimuli which evoke fighting from adult robins, and he found that a bunch of red breast feathers would evoke these threat postures as effectively, or nearly so, as a whole adult bird; in other words, the stimulus which was evoking this ambivalent behavior was a relatively simple one.

*Leake:* It is interesting that this factor of aggressiveness and submissiveness, as it were, in connection with territoriality, has been described now in crickets.

*Livingston:* Is there a way to measure how long the natural internal behavioral patterns in the bird may be disrupted in this way, for example, by finding out how long it is after such an exposure before the bird sings or does something else that he might be likely to have done spontaneously if he had not been interrupted by the presentation of the owl?

*Hinde:* With a long presentation of an owl, for example, 30 minutes, as the mobbing response is waning away, the chaffinch may nip down to the food dish and snatch a few seeds and eat them and then return to his mobbing; so here he is returning to one of his normal maintenance activities.

*Livingston:* But is there anything significant about the time intervals, say, between owl and dog or other stimuli that you find will give rise to this chirping and moving, in respect to the duration of interference with singing or feeding or other behavior of the bird following discontinuation of such disruptive presentations?

*Hinde:* A chaffinch, by itself, feeds on the average about once every 17 minutes. The owl-mobbing response continues longer than that, though when it has lasted about 25 minutes, as I say, he may occasionally feed.

*Fremont-Smith:* Suppose you presented the owl for a very brief time. How long would it be after that before the chaffinch would go back to feeding?

*Hinde:* I haven't tried this. If I understood Dr. Bodian correctly, he said that he was unhappy because I was using this to analyze drive. The whole point I was trying to make was that drive was not a concept that is useful to me in studying the changes in this response.

*Bodian:* Actually, I expressed unhappiness about the use of the call response as a measure of what may be a complex stimulus. It seemed to me that it doesn't discriminate among significant differences in the components of the stimulus.

*Hinde:* But there are no components of stimulus which affect approach or avoidance differentially.

*Reynolds:* The approach is a defensive reaction in a passerine bird, just as much as the avoidance.

*Harlow:* I think there is an interesting, perhaps, unresolvable theoretical point being fought here; that is, whether there are stimuli—and I prefer to call them incentives—which produce or elicit ambiguous responses, that is, both approach and avoidance responses. It is obvious that there is a very broad category of stimuli or incentives which elicit approach responses consistently, just as it is obvious that there is a very broad category of incentives which elicit responses of avoidance consistently.

However, in the case of these ambiguous responses, it is difficult to discover components in the stimuli, some of which cause approach and some of which cause avoidance. Let's not be too sure that one can break down complex stimuli into multiple components. I think that is the point you are making. One cannot describe these kinds of things simply in terms of either the stimulus or the animal. I think you can only describe them in terms of the development of the animal.

For example, in the young monkey at birth, there are no avoidance responses. All stimuli elicit positive responses, unless, perhaps, you count stimuli which can be completely self-destructive to the animal, which we haven't tested.

*Fremont-Smith:* Is this true of falling?

*Harlow:* Falling is not a stimulus of external threat. Falling probably does cause an unpleasantness, but external stimuli elicit an approach response. A loud noise might cause an adversive response. I don't know whether a noise can be made loud enough to cause it. I'm sure things have to be above the tolerance threshold of the organism. There is a submaturational age when these stimuli cause approach, when big objects, flashing objects, moving objects, noisy objects, cause avoidance. Then, perhaps, at a subsequent age, some of them at least will call out ambiguous responses. This is a so-called timidity response in the primate both in the child and in the monkey. I am by no means convinced that there are not ambiguous response patterns that are elicited by stimuli at an appropriate maturational age.

*Fremont-Smith:* Ambiguous as seen by us as adults?

*Harlow:* Ambiguous as involving both avoidance and approach components.

*Leake:* I would like to bring up again the point I made earlier about the characteristics of the responding organism to a constant stimulus. Considering different organisms in the same species, there is a question as to whether the constant external stimulus may not, in some of the individual organisms, be intensified in so far as perception is concerned, and, in others, reduced. The constancy of the stimulus, in other words, should not blind us to the proposition that the way in which the stimulus is handled by different individuals may be different.

In the human adult, we are aware of the fact that there are certain people who do intensify a constant stimulus, whereas others to whom that same stimulus is applied show a reduction in the character, at any rate, of the response. It is well known that this is so in pain. I do not know whether it has been examined with other forms of stimuli. I think it is a point that should be taken into account.

*Hinde:* I think that it is a semantic problem, isn't it? Verplanck (19), when writing about Skinner's work, pointed out the number of different ways in which this term *stimulus* is used. What I meant when I was saying "constant stimulus" was something presented by the experimenter. What you mean is something experienced by the animal. These are two different things.

*Leake:* It is precisely that particular point that I wish to bring out; that is, the stimulus presented by the experimenter may vary in different organisms of the same species.

*Bridger:* In respect to noxious stimuli, human neonates show withdrawal responses to them right from birth.

Also, in relation to Dr. Hinde's experiments, we found in so-called ethological, psychological studies of infants that one of the important factors is the role of the state of the organism at the time when it is being stimulated and the responses are being measured. I was wondering whether the so-called arousal versus inhibitory effects are specific to the owl being presented as the stimulus or whether other kinds of stimuli would also have produced an arousal state in the bird, and hence evoke a greater response than to the dog image, which immediately followed.

We found, for example, that the rooting response in babies is increased with general arousal and not only by hunger. Any kind of stimulus which arouses the baby produces an increased rooting response.

However, in contrast, we also found that at times, when a stimulus had been presented to the oral zone, its next presentation produced increased rooting as compared with stimulating the baby's foot, say by putting it in icy water.

There seem to be, therefore, two types of arousal, one specifically related to the response being elicited, and the other a general arousal. I was wondering in your case whether you had controlled the general arousal caused by the initial presentation of the owl.

*Hinde:* I had not done this.

*Bridger:* Say, making a loud noise and seeing whether that would produce more responses to the subsequent specific stimulus.

*Hinde:* The difficulty with this response is that it is to fear-provoking objects, and any arousal stimulus used comes into the same category, so that general effects cannot be segregated from specific effects in this way.

*Purpura:* Dr. Bridger, are the responses observed in the newborn human infant associated with any specific electrographic alterations?

*Bridger:* I haven't been measuring the EEG on these infants, but I think others have.

*Brazier:* Yes, there is the classic work of Mme. Dreyfus-Brisac (4,5) and of her pupil, Mme. Samson-Dollfus (17). There is also a monograph by Pichot (16). More recent work in this country includes that of Ellingson (6), of Glaser (7) and of the group at the Boston Lying-in Hospital (3). Stimuli do cause EEG changes in the newborn.

*Purpura:* What kind of change is seen?

*Brazier:* It depends on the level at which the child is sleeping, just as in Professor Sokolov's experiments. At a certain level of sleep, a light evokes a K complex, but the infant does not, in common parlance, wake. The arousal type of EEG is more difficult to evoke by a stimulus, but can be obtained and is present as the background when the child is wide awake.

*Purpura:* In the immediate neonatal period?

*Brazier:* Yes.

*Fremont-Smith:* Dr. Bridger said something I would like to emphasize; that is, that the impact of any stimulus is very dependent upon the state of the organism. This we all accept, in a sense, but at the same time we also act as if we believe there is such a thing as a characteristic response to a given stimulus, whether that be a drug or an owl. I think it is of profound importance for us to bear in mind the fact that the state of the organism is an essential determinant of the response, and that if you arrange the state cleverly enough, you may be able to obtain directly opposite responses in the organism to identical stimuli.

*Bridger:* In the case of human neonates, we found that an excitatory stimulus, such as sound, light, or at times even cold water, produced a quieting of the baby if he were already aroused at the time the stimulus was applied. And conversely, warm water, which is usually an inhibitory stimulus when the baby is aroused, produces an arousal response when the baby is quiet.

*Roberts:* Dr. Hinde, I wonder if complete restraint of movement of the bird would affect his response to the stimulus that you present.

*Hinde:* You can't confine the bird in so small a space that it can't fly. If it can fly, then it flies from one side of the cage to the other. There are practical difficulties there.

*Leese:* I think that the analyses of the stimulus given by Dr. Bodian and Dr. Harlow are very important to the whole subject which we have been discussing. Murray (15) made an analysis similar to yours several years ago. He also was making stimulus analyses. He felt that the many facets of a stimulus should be looked upon as a unit, which he called a "press." When man or animal responds to a stimulus, or press, he responds to the sum total of the motivator. Repetition of the press results in increased consistency in response. Professor Sokolov called the resulting behavior habituation. He has observed that very small differences in his stimuli cause considerable change in response.

In Dr. Hinde's experiments, I have some difficulty in analyzing the "press." It certainly isn't just the two circles or eyes which limit the stimulus; the whole bird must be involved in the press situation. There would also be a difference in the owl and the dog because the total presses are different. There must be something phylogenetically specific in the owl stimulus as compared with the dog when these are presented to the chaffinch.

*Lowell:* I agree with Dr. Bodian about trying to restrict this to one area, and I would like to present some material that bears on this point.

I think this will also have some bearing on the kind of presentation which we anticipate from Professor Luria, on the influence of the second signaling system on behavior. This work deals strictly with human subjects (typical college sophomores).

In attempting to objectify the very rich field of projective techniques, we tried to produce systematic changes in objective behavior by the verbal instructions that were given (14). I won't elaborate on that aspect other than to show some scores for projective material. One set of scores is for material written under what we call neutral instructions, just asking the subjects to write a story, and the other scores are for projective material written under ego-involving instructions. The subjects were led to believe that this material was going to be used by the Office of Naval Research to select officer candidates, which at that particular time was a quite important issue for them.

I won't describe any of the sub-categories in Table V, except to point out that under the neutral instructions, where the subjects were asked merely to write a story, we had a mean score of 5, and under the ego-involving or what we called achievement-oriented instructions, this score was significantly greater.

We wanted to demonstrate that this worked not only on college sophomore scores but also on other cultural groups. Table VI shows results from a group of ninth-grade Navaho boys who were given essentially the same instructions, except that we couldn't tell them it was the Office of Naval Research selecting officer candidates. What we did tell them was that we had heard that Navahos were the best storytellers and we wanted to see if they really could tell such wonderful stories. Again, the neutral as opposed to the achievement-oriented instructions produced this significant change.

But with regard to drive and the notion that Dr. Bodian is stating, of trying to relate it to just one area, in an attempt to study achievement-motivation, we constructed two tasks which we administered to test some common notions about the effect of motivation on both learning and performance (Table VII). We constructed a scrambled word test, which required that the subject rearrange the letters to make a simple four- or five-letter word. This is a task in which some learning could take place. If we divide the groups of college students into those with high, and those with low achievement motivation scores, as measured projectively by these categories which we have previously demonstrated to change with verbal instruction, we find that the mean difference in score between the two groups increases systematically with time (Table VII).

## TABLE V

**Frequencies of Types of Achievement Imagery Appearing in Stories Written by Twenty-one Male College Students Under Neutral- and Achievement-Oriented Conditions (Total: 63 Stories, 3 per Student)**

| | Neutral | Achievement-Oriented |
|---|---|---|
| Achievement imagery | 30 | 46 |
| Doubtful imagery | 21 | 14 |
| Unrelated imagery | 12 | 3 |
| Need | 14 | 25 |
| Instrumental activity | 14 | 18 |
| Personal obstacle | 4 | 6 |
| Environmental obstacle | 2 | 10 |
| Anticipatory goal states | | |
| Positive | 7 | 14 |
| Negative | 5 | 7 |
| Affective states | | |
| Positive | 9 | 17 |
| Negative | 1 | 4 |
| Nurturant press | 4 | 6 |
| Achievement thema | 28 | 40 |
| Mean achievement score | 5.05 | 9.05 |
| Mean difference | 4.00 | |
| *SE* difference | 1.09 | |
| *t* (paired differences) | 3.67 | |
| *p* | <.01 | |

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## TABLE VI

**Frequencies of Types of Achievement Imagery Appearing in Stories Written by Twenty-one Ninth-Grade Navaho Males Under Neutral- and Achievement-Oriented Conditions (3 Stories per Student)**

| | Neutral | Achievement-Oriented |
|---|---|---|
| Achievement imagery | 17 | 32 |
| Doubtful imagery | 21 | 21 |
| Unrelated imagery | 46 | 31 |
| Need | 6 | 16 |
| Instrumental activity | 6 | 11 |
| Personal obstacles | 3 | 1 |
| Environmental obstacles | 2 | 0 |
| Anticipatory goal states | | |
| Positive | 2 | 4 |
| Negative | 1 | 1 |
| Affective states | | |
| Positive | 2 | 7 |
| Negative | 1 | 1 |
| Nurturant press | 2 | 2 |
| Achievement thema | 2 | 15 |
| Mean achievement score | −.10 | 2.81 |
| *SD* | 3.15 | 3.42 |
| Mean difference | 2.90 | |
| *SE* difference | .88 | |
| *t* (paired differences) | 3.30 | |
| *p* | <.01 | |

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## TABLE VII

### Mean Output of Scrambled Words per 2-Minute Period for Subjects with High and Low Achievement Scores

| | 2-Minute Periods | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *1* | *2* | *3* | *4* | *5* | *6* | *7* | *8* | *9* | *10* | Total |
| High achievement ($N = 19$) | 9.2 | 10.4 | 11.5 | 11.2 | 11.6 | 11.8 | 12.2 | 10.9 | 12.0 | 12.9 | 113.7 |
| Low achievement ($N = 21$) | 9.9 | 9.5 | 10.1 | 10.1 | 10.4 | 10.8 | 10.4 | 9.6 | 9.6 | 10.3 | 100.8 |
| Mean difference | .7 | .8 | 1.4 | 1.1 | 1.2 | 1.0 | 1.8 | 1.3 | 2.4 | 2.6 | 12.9 |

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Figure 136 shows this a little more clearly. This is a graph which presents these same data; it shows learning under the influence of this higher motivation.

Then, in a task of adding three 2-digit numbers where, presumably, one would not expect much learning to take place in a test of college students, we find merely greater output throughout, fairly stable performance but higher output, for those who had high achievement motivation (Table VIII). These college students were equated on ACE (American Council on Education) scores, as far as their quantitative abilities went. I think, therefore, if we try to study drive restricted to a particular area, achievement motives, and then try to see its application in different aspects but related only to that particular motivation, perhaps Dr. Bodian's point is quite relevant.

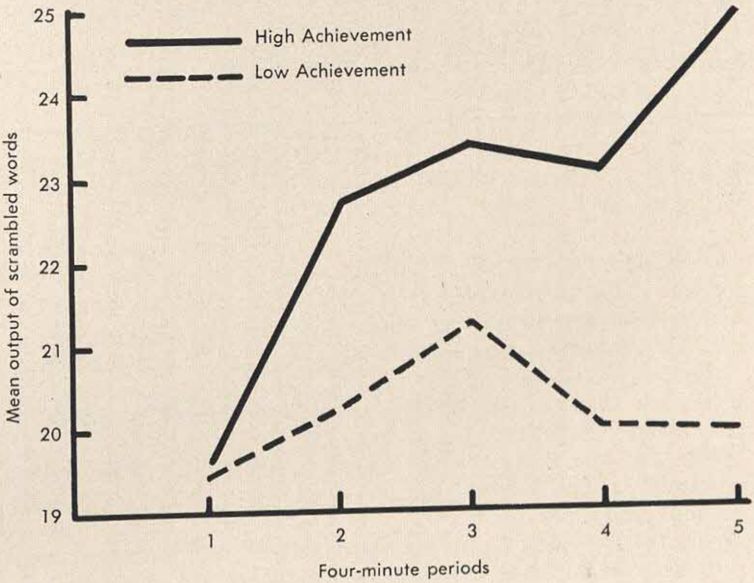

FIGURE 136. Mean output of scrambled words per 4-minute period for subjects with high and low achievement scores. Reprinted, by permission, from McClelland, D., Atkinson, J., Clark, R., and Lowell, E.: *The Achievement Motive.* New York, Appleton-Century-Crofts, Inc., 1953.

## TABLE VIII

### Mean Number of Addition Problems Solved per 2-Minute Period for Subjects with High and Low Achievement Scores

| | 2-Minute Periods | | | | | |
|---|---|---|---|---|---|---|
| | *1* | *2* | *3* | *4* | *5* | Total |
| High achievement ($N = 19$) | 31.6 | 32.7 | 29.9 | 31.5 | 31.7 | 157.4 |
| Low achievement ($N = 21$) | 26.7 | 26.7 | 25.0 | 26.2 | 26.0 | 130.6 |
| Mean difference (H-L) | 4.9 | 6.0 | 4.9 | 5.3 | 5.7 | 27.8 |

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## REFERENCES

1. AHRENS, R.: Beitrag zur Entwicklung des Physiognomie - und Mimikerkennens. *Ztschr. exper. ang. Psychol.* 1, *412-452* and 2, *599-633 (1954).*
2. BLEST, A. D.: The function of eyespot patterns in the *Lepidoptera. Behaviour* 11, *209-256 (1957).*
3. BRAZELTON, B., GALLANT, D., and STECHLER, G.: *Proc. Symp. on Research in Infancy and Early Childhood.* Boston Univ. 1960 (In press).
4. DREYFUS-BRISAC, C., SAMSON-DOLLFUS, D., and FISCHGOLD, H.: L'activité électrique cérébrale du prématuré et du nouveau-né. *Semaine hôp. Ann. de Pediat.* 31, *135-142 (1955).*
5. ———: Technique de l'enregistrement du prématuré et du nouveau-né. *EEG Clin. Neurophysiol.* 7, *429-434 (1955).*
6. ELLINGSON, R. J.: Electroencephalograms of normal, full-term newborns immediately after birth with observations on arousal and visual evoked responses. *EEG Clin. Neurophysiol.* 10, *31-50 (1958).*
7. GLASER, G. H.: The neurological status of the newborn; neuromuscular and electroencephalographic activity. *Yale J. Biol. & Med.* 32, *173-191 (1959).*

8. Hartley, P. H. T.: An experimental analysis of interspecific recognition. *Symp. Soc. Exper. Biol.* **4**, *313-336 (1950)*.
9. Hinde, R. A.: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaffinch (*Fringilla coelebs*). I. The nature of the response, and an examination of its course. *Proc. Roy. Soc. London B.* **142**, *306-331 (1954)*.
10. ———: Factors governing the changes in strength of a partially inborn response, as shown by the mobbing behaviour of the chaf- *Roy. Soc. London B.* **142**, *331-358 (1954)*.
11. ———: Alternative motor patterns in Chaffinch song. *Animal Behav.* **6**, *211-218 (1958)*.
12. ———: Unitary drives. *Animal Behav.* **7**, *130-141 (1959)*.
13. Lack, D.: The behaviour of the robin. *Proc. Zool. Soc., London. A,* **109**, *169-218 (1939)*.
14. McClelland, D. C., Atkinson, J. W., Clark, R. A., and Lowell, E. A.: *The Achievement Motive.* New York, Appleton-Century-Crofts, Inc., 1953.
15. Murray, H. A.: *Exploration in Personality.* Chapt. II. London, Oxford, Univ. Press, 1938.
16. Pichot, F.: *Contribution à l'Étude de l'Électro-encéphalogramme Normal et Pathologique de Nouveau-Né.* (Thesis) Toulouse, Fournie, 1953.
17. Samson-Dollfus, D.: *L'Électroencéphalogramme du Prématuré jusqu'à l'âge de Trois Mois et du Nouveau-Né à Terme.* (Thesis) Paris, Foulon, 1955.
18. Thorpe, W. H.: The learning of song patterns by birds, with especial reference to the song of the chaffinch, *Fringilla coelebs. Ibis* **100**, *535-570 (1958)*.
19. Verplanck, W. S.: In Estes, W. K., *et al.*: *Modern Learning Theory.* Chapter on B. F. Skinner. New York, Appleton-Century-Crofts, 1954 (pp. 267-316).

# AFFECTIONAL BEHAVIOR IN THE INFANT MONKEY

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I PREFER the phylogenetic or ontogenetic approach, so I shall discuss the ontogenetic development of this research. About 6 years ago, we began to separate baby monkeys from their mothers on the first day of life, usually within 12 hours, and then to study them. When we started, our only goal was to study the maturation of learning, and this is all we did for 6 years. We now feel that we have amassed a very considerable amount of information on the maturation of learning in the monkey. This is a very orderly type of procedure in which more and more complex learning capabilities evolve with time. It appears that the monkey is an animal which is capable of learning simple things like sound-pain conditioned responses in the first 2 or 3 days of life, and probably attains full intellectual maturation at about 4 years of age or at about the time the male becomes sexually mature. According to the Binet test, this is also true of man. There is an amazing similarity between man and monkey. Actually, a study of any behavior pattern, for example, emotional patterns like anger or fear, will show a surprising similarity in maturational development between man and monkey. I think that the baby monkey in its first year of life differs from the human being in three ways: The monkey is born more mature; it grows up faster; and it is much more intelligent than the human baby in the first year of life. But don't think the infant monkey is far from nonsentient. It probably has far more capability of imaginative thought than the year-old human infant. However, the human infant is superior in one way, in that it has the potentiality of being subsequently superior. The baby is beginning to develop language, but the language is unrelated to intelligence. The baby's language is at about the level of the mynah bird's; that is, it does not age intellectually in any way.

When we originally started to try to study affection 3 years ago, we set out with just one goal; that was to try to analyze the affectional responses of the mother and infant, using surrogate, or artificial, mothers. Our long-term goal, as part of this program, would eventually, be to study all the affectional systems that can be discovered in the monkey, both with artificial and real mothers, real playmates, and perhaps artificial playmates.

We would hazard the guess that there are at least four quite separate affectional systems: the system that binds the infant to the mother, the system or systems between infant and infant, and the system that binds the adolescent to the adolescent. This is followed by what is called the population explosion, and, as a result of this, there is the fourth system, the one that binds the maternal affection of the mother to the infant. I think that there are very likely other systems and that probably you will find there is a separate system of affection between the adult male and the young infant. Field studies begin, I believe, to supply us with evidence that such a separable system exists.

I have little to say, except to mention that research is just beginning, on anything other than the affectional system that binds the infant to the mother. We hazard the guess that each of these affectional systems can, within limits, be broken down into developmental stages but cannot really be understood until their ontogenetic development has been traced. I don't mean to imply that these stages are separate in time; they are obviously overlapping. But I believe, within limits, one can break these down into stages, and there is something to be gained by this particular device.

In the case of the infant's affection for the mother, I would classify the first stage as a simple reflex stage. It probably ends somewhere between day 10 and day 20 of life. This is followed by an attachment stage, a security stage, and then a separation stage. Of course, the monkey infant is physically and, perhaps, psychologically separated from the mother, after it reaches about 2 years of age or perhaps more.

The reflex stage begins at day 1 and continues up to day 20. We don't know for certain. This probably depends upon the measure one takes.

*Fremont-Smith:* And the attachment stage goes from when?

*Harlow:* The stages from here on are overlapping and must be defined in terms of criteria. For example, in our learning studies, we have found that, aside from necessary reflexes, there is no such thing as a critical period coming in on a particular day. In learning, one has to think of a critical *stage.* There is the earliest time that an animal can learn a problem of a certain level of difficulty with unlimited experience, and then the age at which the animal learns this same problem with absolute maximum efficiency, that is, as fast as an adult can. With each of the learning tests we have, we think one can define this by a dimensional critical stage.

. Figure 137 shows a one-day-old baby monkey clinging to a soft cloth. Notice its facial expression. Figure 137 also gives some idea of the developmental status of the newborn monkey. The newborn infants weigh somewhere between 11 and 22 ounces. About 16 ounces is a mean weight.

*Magoun:* Is this monkey vocalizing?

*Harlow:* Yes, it is vocalizing. This is the first day of life. The mother monkey apparently has a very special call for summoning her young infant back whenever it gets away from her. She also has a very special kind of expression. We think it is an ameliorated fear gesture. We never really tried to make a systematic study of the vocalizations in the monkey, although we have some interest in doing so

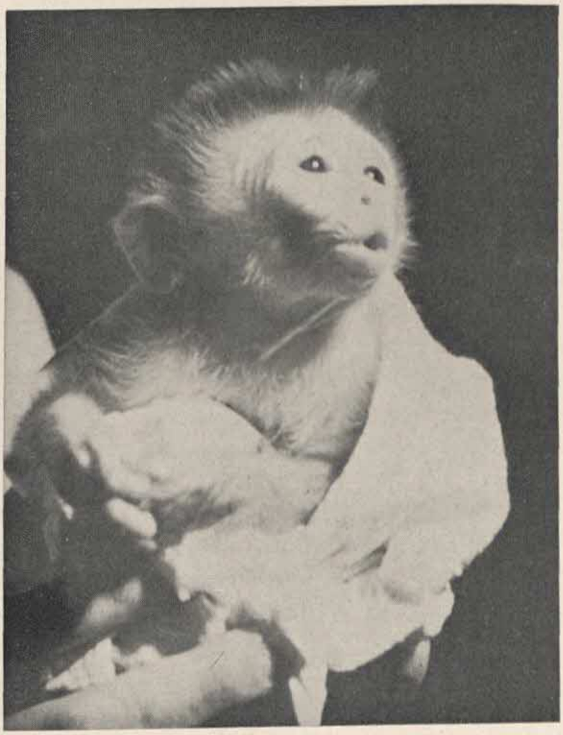

FIGURE 137. One-day-old monkey.

now. We expect, in some of our tests, to use certain kinds of maternal calls, to see if we can influence the infants by these kinds of vocalizations.

Theoretically, at least, there should be two systems that attach the infant to the mother. One is what, using Bowlby's (2) term, we call contact-comfort, just sheer responsiveness to the contact of the mother's body. The other theoretical system relates to the breast, the act of nursing. On the first day of life, certain reflexes that apparently operate within these systems can be observed. If a newborn monkey is put on his back, the animal rights himself; in other words, the righting reflex is present in the first day of life. Some of the monkeys can vaguely locomote on the first day of life, and most of them can locomote with some success by the 5th day of life. If, however, you put the monkey on his back and give him a soft piece of cloth, he clasps the cloth without changing his position. The righting response has been overridden. No attempt to right is made as long as he has the cloth; he clings in this posture as he would cling if attached to the mother's belly. This is on the first day of life. In other words, this is a reflex which is going to operate to give the contact-comfort variable that Bowlby (2) and others have written about.

*Fremont-Smith:* Why do you say "reflex"?

*Harlow:* Isn't it a reflex? This is an automatic, uncontrollable response on the part of the animal. The stimulus comes and he automatically moves. He has no option. Actually, if these animals, while they are on their backs, happen to make contact with one hand on the other or one foot on the other, this will also override the righting response. They will maintain this posture too.

*Bridger:* Does this response habituate out? For how long in its development does the baby hold the wire cloth?

*Harlow:* I will answer that in a moment. There is also the response that is going to lead to sucking; that is, if the upper lip of the newborn monkey's mouth is stimulated he grasps the finger and sucks. Theoretically, this reflex mechanism certainly should serve the activities associated with the breast and ingestion of fluids.

One of the reflexes of the monkey is upward climbing. When put on a hardware cloth surface like the one shown in Figure 138, and as long as his head is oriented upward, he will climb to the top. As a matter of fact, he will climb right over the top. We think that this reflex serves a monkey in that as long as he makes contact with the mother's body, he will climb upward to a position on the thorax until he is restrained by

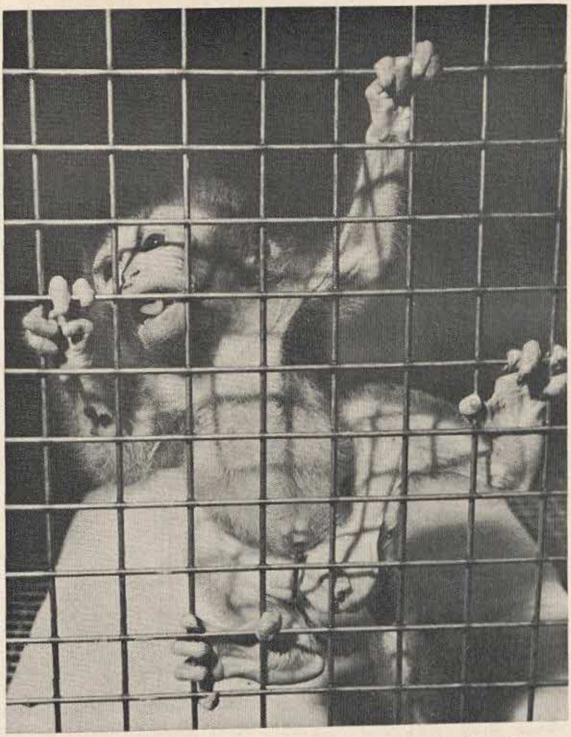

FIGURE 138. Infant monkey showing upward climbing reflex.

the mother, so this might well be a reflex important to the survival of the animal.

*Fremont-Smith:* How soon after birth does this happen?

*Harlow:* Most monkeys can climb at one day of life. In the case of the monkey—and of course, it is true of the human child—climbing precedes four-footed or two-footed locomotion.

*Fremont-Smith:* If the hardware cloth is laid flat, instead of vertically, will the monkey still move along it? If you turn this to one side, he would then put himself in a vertical position again?

*Harlow:* Some of our very young monkeys, if the head is down, will orient the head and climb, but others will not orient the head themselves. It may have something to do with the stage of maturity at which they are born.

*Fremont-Smith:* So it is not necessarily upward climbing, then?

*Harlow:* I think it is. We put animals on a hardware cloth on the cage, which is flat, and they don't climb across it with anything like climbing proficiency. When there is an opportunity for upward climbing there seems to be a kind of forced behavior.

A very dramatic and interesting response, sometimes seen and sometimes not, is the "following response." Most animals have to be more than one day of age before it appears and it isn't as reliable a response as the others. If an animal that is apparently almost immobile and doesn't really locomote at all is put on a table, and a piece of cloth is placed against the upper part of his face and is then gradually withdrawn, the animal automatically follows, sometimes quite rapidly. He suddenly has amazing locomotive ability; he will follow the cloth right up to the edge of the table.

A reflex familiar to all is the reflex of forced grasping. A cylindrical surface is placed against the palm of the animal's hand, and the monkey —and, of course the human baby—clasps it and is completely unable to let go. We think that the reflexes we have shown and discussed previously belong in the same category as this reflex. Until very recently, we thought that these contact reflexes—where cloth is placed against the surface of the monkey's body and the righting response inhibited— would only be elicited by some soft substance. This is not true. Any contact substance inhibits the righting response in the very young animal, probably under 10 days old (although we are just beginning to get the developmental data on this). In other words, when a cylinder of wire is placed on the ventral surface of the very young infant, he will grasp the wire and make no attempt to right. Indeed, what is apparently an adversive contact substance like very rough emory cloth or sandpaper will call out the clinging response. The animal will not right itself.

*Hess:* How about hot and cold?

*Harlow:* We haven't tried hot and cold. I am sure that temperature is a variable of importance in the very young animal. With this grasp response, I have observed something very interesting. In a social testing situation, we had a kind of climbing chair, and I saw a baby monkey, 15 days of age, sitting across one of the rungs of the chair. He seemed to be trapped, and he was screaming and crying continuously. Yet, he didn't seem to be wedged in, in any way. What had happened to this unfortunate infant was that he had gotten his hand across a rung in this chair device, and, of course, when his hand hit the rung, the hand clasped down; it was just as though he were handcuffed. The monkey was obviously trying to get out, but could not. This gives us a good definition of a reflex—an act which traps the animal. In this case, even though the infant wanted to go out and explore, he couldn't. We can't say exactly when wire and sandpaper will no longer call out the grasp response, but we think that these reflexes drop out somewhere between 10 and 20 days and, after that, they are no longer simple reflexes. Whatever the mysterious difference is between reflex and voluntary, this difference exists.

*Reynolds:* Can you substitute grasp of one hand for grasp of the other? In other words, if you give him something to hold in the other hand, can he release the first one more readily?

*Harlow:* I have never tried that. I don't know.

*Kelly:* Isn't this automatically involved in climbing?

*Harlow:* You might well ask why don't they become immobilized when they climb up this hardware cloth surface and wrap their hands around the rung? They don't, and I don't know why. Probably, it is necessary to stimulate more of the palm of the hand to evoke the tight, immobile reflex of the grasp response. A considerable surface must be affected, so if a monkey were just climbing up, using the tips of his fingers, this wouldn't happen.

*Sokolov:* Have you tried to study the region from which this reflex can be produced? How far from the palm does this reflex excitatory region extend?

*Harlow:* The idea that we might be able to define these various kinds of reflexes, some relating to nursing and some relating to contact, came to us only at the end of last year, and before we could analyze these reflexes, we had to wait for this year's baby crop. The first real attempt to do this systematically has just barely started. We have certain ideas; for instance, we think that for touch, the upper part of the mouth calls forth the response more than the lower part. We think that this matter of touching with the cloth may relate to the rooting reflex, where the animal doesn't really touch the nipple, but he buries his head in the body wall of the mother. We are quite interested in continuing research on this question of reflexes.

*Windle:* Dr. Harlow, you mentioned that you had to wait for this year's baby crop. Do you have a seasonal harvest?

*Harlow:* Yes, we have a seasonal harvest.

*Windle:* That is very interesting, because, at our laboratory in Puerto Rico, we do not.

*Harlow:* We think that these great complex patterns, like the adolescent-adolescent pattern, may in part be culturally determined, even in the monkey. Maybe this seasonal conception is part of it, too. We tend to have a period from July to October in which there are either no babies or very few babies. These things are complicated behavior patterns. The peak for births tends to come in April, or close to it.

*Keller:* Do you have a 100 per cent baby crop?

*Harlow:* We are harvesting about 70 per cent babies per year per female.

Now we can start on our official experiment which we originally designed to see if we could determine the relative importance of the so-called contact-comfort variable as contrasted to the ingestion of milk and activities theoretically associated with the breast. Figure 139 shows an infant monkey in the situation we devised.

The basic experiment used eight animals for whom we fabricated artificial mothers: a cloth mother, called our "good mother," and a wire mother, called our "bad mother." In our latest form, the cloth mother is nothing but a wire mother with a terry cloth sheath pulled over the body. The faces differ, and I'll be glad to go into this. On the cloth mother we deliberately constructed a face which we were quite sure would be a fear stimulus. As a matter of fact, we have now tested some 70 to 80 day-old monkeys with this face, and have proved that we were

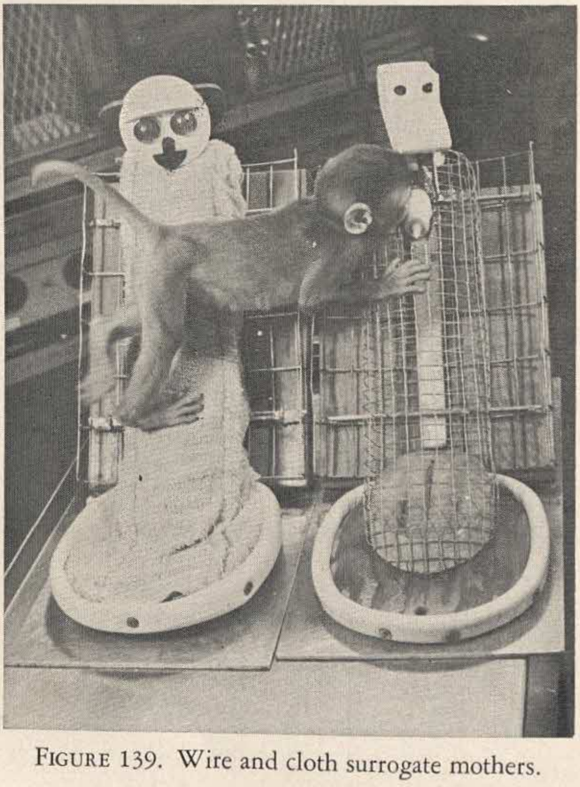

FIGURE 139. Wire and cloth surrogate mothers.

completely successful. This face, to an animal that has never seen it before, is quite a terrifying experience.

Four of the babies got all their food from the cloth mother, and four other babies got all their food from the wire mother. A cage was attached to the surrogate compartments, and for the first 15 days of life the animals had a heating pad and could stay on it or go to either surrogate mother, as they wished. The first measure that we used to try to show differential preference or affection was simply the amount of time they spent on each of the two mothers. This was automatically recorded.

On alternate days, the mothers were moved back and forth to prevent the formation of position habits. A typical response of a young monkey to the cloth mother was to snuggle into the base of the surrogate. Probably we angled these surrogates up too steeply for immature animals, since the mothers do not have arms. It is not as simple to make a surrogate with effective arms as it might sound.

As the animal gets older, it tends to spend more and more time on the thorax of the surrogate mother. At somewhere between 20 and 30 days of age, the baby monkeys begin to develop an intense interest in the face, with a great deal of manipulation of the face, and when their teeth come in, since the mother can't bite back, they chew the faces apart and pluck out the eyes. It's all done in a spirit of deep affection, I'm sure.

*Sokolov:* You have now shown that the towels produce the same response, but have you studied what the elements of this complex stimu-lation are and if they are important for the reproduction of this response? Is the face necessary for this reaction?

*Harlow:* No, the face is absolutely unnecessary. You can have a faceless mother or a ball for the face; it makes absolutely no difference. We merely put the face on because sooner or later we want to analyze the responses to the face. Just as in the human child, the response to the face comes in at 6 weeks to 2 months.

*Sokolov:* What is important? A certain kind of material which is in contact with the monkey?

*Harlow:* That's right. We can say certain limited things about the material. We know, for instance, that cheese cloth would probably be just as good as terry cloth.

*Sokolov:* But a stone doesn't produce this effect?

*Harlow:* Stone? I'm sure that stone wouldn't do it.

*Fremont-Smith:* The wire is just as good as the cloth?

*Harlow:* No. Let me explain. I'm sure that any soft cloth-like or fur-like substance will produce this response; in other words, cheesecloth, terry cloth, and spun nylon all do well. We chose terry cloth for sanitary purposes, as the surrogate must be laundered once a day. Furthermore, the terry cloth is rough and it provides the animal with a good deal of physical support. It isn't, of course, comparable to the wire in this regard, as the wire is an excellent substance for grasping.

I shall return to this very shortly. We hope to learn more about the quality of the substance that will inhibit the righting response. That, I think, is a way to study textures. Just as we think the response to the wire is going to disappear in days, a difference in the texture of the cloth may hold this response for a longer period; I don't know.

*Field:* Can they get milk from that surrogate mother?

*Harlow:* All the milk they get throughout their lives comes from one surrogate mother or another. We have other conditions; we have babies who are served on a single cloth lactating mother and others on a single wire lactating mother from birth on.

I have already discussed the response of stimulating the face, which calls out head-turning and enables the baby to latch on to the nipple; however, we had missed the fact that this response also apparently is called out by any substance early in life, not necessarily a soft substance like a cloth or a finger. Early in our efforts to rear monkeys, we put babies in hardware cloth cages and we realize in retrospect that in the first 10 or 15 days of life they would go up and touch their noses and their faces to the hardware cloth. This automatically would call out these turning responses, so some of our babies almost rubbed their noses off before this response to a hard substance stopped calling out this head-turning and nipple-searching.

Often, in the first few days of life, the animal must be given some support to enable him to nurse but usually by 4 or 5 days of age he can climb up the surrogate and nurse independently.

Figure 140 shows our basic data, in terms of time spent on the cloth mother and the wire mother for infants that fed only from a cloth mother and those that fed only from a wire mother. First, let's take the time spent on the cloth mother by infants fed entirely on the cloth mother. As can be seen, quite early in life, these animals are spending 16 or 17 hours a day, continuously, on the cloth mother. After the first 25 days of life, it doesn't make any difference whether they are nursed on a cloth mother or a wire mother; the differences are slight and not statistically significant. We believe that even more striking are the data of the amount of time spent on the wire mother. The animals fed on the cloth mother spend very little time with the wire mother, which, of course, causes no surprise whatsoever. The striking thing is that animals fed on the wire mother spend practically no time on the wire

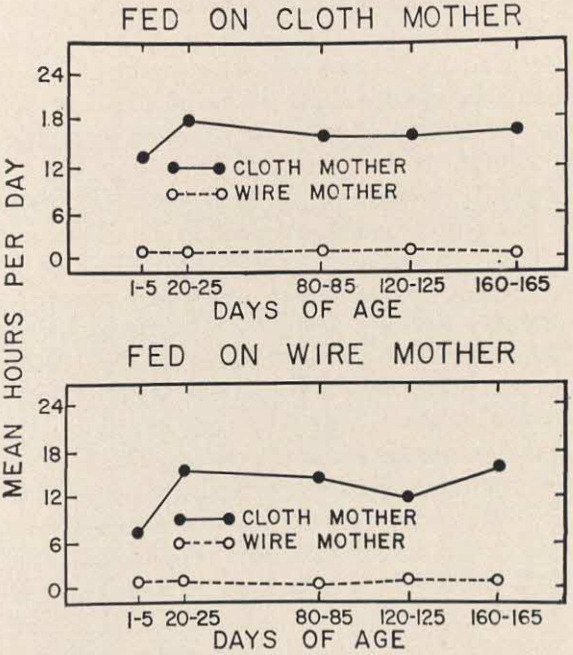

FIGURE 140. Time spent on cloth and wire surrogate mothers.

mother. It is as though some animals catch on to when the feeding period is going to come and, a few minutes before they are going to be fed, they change over. There is no indication that the baby fed on the wire mother goes to it for any affectional purpose.

*Windle:* How many animals were there in this series?

*Harlow:* In this particular experiment, there were four animals fed by each surrogate mother. Four and four. However, we have many other experiments. We have now run some seventy animals in one form or another on these surrogates. There is a very small standard deviation. There are individual differences, of course, but we approach an all-or-none phenomenon.

*Sokolov:* I am interested in the constellation of stimuli important for this reflex. I believe that the degree of temperature produced by the cloth mother may be of importance in this case. Have you tried different temperatures of the cloth mother for the duration of these contacts?

*Harlow:* Yes, we do have a control experiment on temperature. A number of friendly cirticisms were made of our previous failure to control certain variables in the cloth and wire mother situation. One of these was that there might be a temperature factor, in that the animal hugging against the cloth mother might increase the temperature, whereas this would not happen with the wire mother. We doubted this because we had seen animals leave the heating pad before 15 days of age in order to attach themselves to the cloth mother. But observation is not an experiment.

Another criticism was that the faces of these two mothers differed. It seemed to us that this could not account for the results, since the animals early in life are not really responding to the face.

Another interesting comment, and a perfectly correct one, was that the cloth mother has a greater capability of becoming urine-soaked than the wire mother, and olfaction might be a variable operating here. Of course, it is perfectly true that this is a theoretical possibility.

It is impossible to test all three of these possibilities at once. An accurate temperature analyis must be done separately, but we did devise a crude type of control experiment. We created a situation with a cloth mother as one of the surrogates; the other surrogate was a cloth mother with hardware cloth circling her body, so that the infant could not contact the cloth, but the cloth could soak up urine very well. We made the faces identical, either the two ornamental faces or the two nonornamental faces. We also put a heating element down the noncloth mother, so that it was something like 7 degrees hotter than the room temperature.

The results were interesting. We got a good deal of individual difference under these circumstances which continued for 15 to 20 days. The animals then went to the cloth mother and stayed with the cloth mother.

*Fremont-Smith:* What did the animals do in the first 15 days?

*Harlow:* Either they showed fairly random behavior—although these data have not been analyzed, we can interpret them fairly well—or else they showed a clear-cut preference for the warm mother. Again, we think this is one of the reflex variables, and these variables collapse between 15 and 20 days. Then the responsiveness is seen, or the same kind of selective responsiveness to the cloth mother observed in the other experiments.

*Sokolov:* Since tactile stimulation is connected with some sex reflexes, it may be that in these emotional reactions, there is some connection between the tactile stimulation and the emotional system.

*Harlow:* A month ago we would have said that sex responses to the cloth surrogates were not obtained in the infant male monkeys. Until less than a month ago, we had never seen sexual responses until the animals were approximately 6 months of age. But we had an atypical little baby—perhaps there was something wrong with his pineal gland—who showed masturbation at the age of about 10 days; so it does occasionally occur. Ordinarily, however, there is no sex behavior until about 6 months of age, long after the infant-mother pattern has been entirely established. I wouldn't question the fact that sex behavior may come in as a supportive response, but I don't think it is a prime elicitor of this kind of behavior.

*Fremont-Smith:* How many infant monkeys have you been able to study?

*Harlow:* No. 140 was born very recently, but the first sixty or seventy were not used on these experiments on affection at all. Certainly, not less than seventy animals have been used in one variant or another of this kind of experiment.

*Hinde:* In this lack of sex behavior, you're not talking about animals reared on the surrogate mother, are you?

*Harlow:* We are talking about animals reared on the surrogate, yes. We have only the most cursory data on animals reared by their own mothers. We are now systematically studying this. We think we're going to have a fairly complicated situation, where we are going to study not only infant-maternal affection, but also the development of infant-infant affection, with identical situations for animals on real mothers as for animals on cloth mothers. We have some concern as to the animals having a pathologically strong attachment to these surrogates.

*Reynolds:* Do you mean by that, more than to a normal monkey mother?

*Harlow:* Yes. They may be completely fixated to such a degree that they have real difficulty in forming normal infant-infant affectional responses. This is the criterion I would take. Actually, we do not have our data on the infant-infant pattern developed to the point that we can really analyze them.

*Sokolov:* In some of the contacts, I would expect that a critical area of surface contact between the baby and the artificial mother would be important for the production of this reaction.

*Harlow:* That's right. We have never tried to find out how small a surface would suffice. Certain problems arise, because clinging also becomes either a variable in its own right or a variable which enhances the contact variable. However, we will try to present some data on this.

*Windle:* How do they behave on the surrogate mothers? Do the infants begin to suck their fingers?

*Harlow:* Yes, very early. There is a great deal of nonnutritional sucking.

*Windle:* Did you see any difference between that on the surrogates and before you began using the surrogates? In the natural situation, this is something that is almost never seen.

*Harlow:* That's right; the babies with real mothers don't suck their thumbs. On the other hand, we are convinced from watching them that they do a great deal of nonnutritional attachment and semisucking at the breast. You can differentiate, you see, any time they go and attach to the breast.

One thing I would like to emphasize is that whether or not we find that sucking is a variable of great importance in the formation of affection, the Rhesus monkey is an extremely oral animal. He engages in about a third as much oral exploration as manual exploration. We don't know, in our babies raised on surrogates, whether the nonnutritional sucking is primarily a function of the lack of a real mother or whether it is a function of the nursing schedule. We have not yet put the animals on the surrogates on a demand schedule, which we certainly will do as soon as we have enough babies. On the natural mother monkey, the baby is really on a demand schedule 24 hours a day. These animals on the surrogates have been run on a fixed schedule.

*Fremont-Smith:* What is the schedule, roughly?

*Harlow:* The babies start off at around eight o'clock, on a 4-hour schedule. The twelve o'clock schedule is out by the fifth day, and they make an easy adjustment. Then, there is a drop to seven feedings a day for quite a period of time, and gradually the number of feedings is cut down.

*Leese:* If surrogates are switched, does it make any difference to the babies?

*Harlow:* Although we don't have any absolutely definitive data, I would say surrogates can be switched at will. Certainly, in the case of the young animal, even surrogates made of different colors of terry cloth can be switched, with no effect. Nor do surrogates with different heads have any effect. Even surrogates without heads make no difference. There probably is a developmental stage when switching the heads at least would no longer work, but, early in life, if you want to make this distinction, the babies are attached to any mother, any adequate mother surrogate, not to a special one.

One thing we are studying eagerly is the attachment to the real mother. We want to find out if and when, and we think it is merely a question of *when*, the infants really develop a specific attachment to a specific mother.

*Hess:* Do you have any idea when this might be, even a guess?

*Harlow:* I don't yet know that it is true that they develop this specific attachment. Our observations are that, early in life, it is the mother who is retrieving the infant, not the infant retrieving the mother. I believe that these animals are going to develop specific affections.

*Hess:* I think one possible guess might be that this would perhaps occur at that time when they might normally show fear responses to these faces. Or sometime just previous to that. That is just a guess.

*Harlow:* Yes. Actually, there are a few data that bear on this. According to S. A. Altman,* the baby monkey, when its next sibling is born, still stays in the geographical region of the mother. This indicates that, by this time, it has obviously developed an affection for a specific mother.

*Windle:* It can go even further. You will see family groups, a pregnant mother with a baby clinging to her, a 1-year-old baby immediately in the offing, and a 2-year-old baby beyond that.

*Harlow:* That's fine. Anyway, S. A. Altman says, and I think it is very interesting, that the original infant-infant contacts in the wild are contacts of the new baby to the 1-year-old baby.

*Fremont-Smith:* The interaction process between mother and infant is, of course, excluded here? You are isolating it, so you're getting an infant reaction against an inert object. But it is quite possible that several time relationships would be different with a responsive mother.

*Harlow:* Yes, completely different. I first presented this material with much enthusiasm, and a child psychiatrist suggested to me that the cloth mother was not a very subtle animal. After having been reminded of this enough times I took it to heart. One of the obvious functions, in what little we have seen of the real mother as contrasted to the cloth mother is that she takes some active part in separating the baby from her. You can see a good mother monkey agonizing as to whether she should let her baby go out and explore the world or whether she should continue to clutch it to her body.

*Fremont-Smith:* The grooming process and all the functions that the mother performs will operate to reinforce this.

*Harlow:* We have some ideas about what happens to babies that are not raised on real mothers, although we don't know whether this is because they aren't raised in real families, or on real mothers.

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*Personal communication.

The most striking fact shown in Figure 140 is that even the babies that are fed all their food by the wire mother, throughout the 165 days spent in this situation, show no tendency to go more and more to the mothers that nursed them. All the situations are here for secondary or derived motives, everything is set up to achieve them, and they simply don't happen. The conditioning process of sight of the mother to active nursing apparently has produced nothing. The only adverse effect we have observed is that when the wire is in the cages and the animals rub their noses on it, they chafe their noses a little. But in our playroom situation for infants, it makes a fine exploratory substance.

*Reynolds:* Although you say there is no statistical difference between these curves, the open circles are, in all cases, above the closed circles. Is that the time spent in feeding that is involved there?

*Harlow:* The feeding time is excluded.

*Bridger:* You mentioned that at birth the infant grasped the hardware cloth and there wasn't any difference?

*Harlow:* That's right, on these reflex tests.

*Bridger:* When do they start showing the difference? When do they start showing a response to an adversive stimulus? It may be the time when they show the differentiation between the soft cloth and the hardware cloth.

*Harlow:* I really can't answer the question, because these studies were done 2 years ago, and the idea of trying to analyze these early reflexes is new, so we have only scattered observations. We have now set up formal experiments, but the first animal went on to the formal experiment one day before I came here.

*Bodian:* Dr. Livingston and I were wondering as you talked whether the babies were always well fed, or whether hunger would make a difference?

*Harlow:* We have babies raised on a single cloth mother and babies raised on a single wire mother. The babies raised on a single wire mother drink as much milk and ingest as much food as the babies raised on the cloth mother. They gain the same amount of weight, so that they are physically healthy. The only difference we found was that when a careful rating of consistency of stool was made, the babies raised on the wire mother had looser stools than the babies raised on the cloth mother. Whether or not this will hold in the future, I don't know.

*Bodian:* There was a question about the time spent on the mother, whether that would vary if one put them on a different feeding schedule, so, perhaps, they were always a little hungry on the cloth mother.

*Harlow:* They are all on the same feeding schedule. At best, they are on a 4-hour schedule during the day.

*Fremont-Smith:* You haven't been able to follow them to see what their sexual behavior is as they grow up?

*Harlow:* We have some scattered data on it.

*Fremont-Smith:* Does it show any difference at all?

*Harlow:* We have data on sexual behavior of babies raised from birth in cages, in which they could see other babies but not make contact. This produces adversive effects on the sex patterns, particularly the pattern of the male. We don't know, in the case of either the male or the female, whether these are irretrievable patterns if the animals are allowed a relatively normal life later on.

*Fremont-Smith:* What about the difference in mothers? What about babies raised on the cloth as compared with those raised on hardware mothers?

*Harlow:* We don't know. From what little data we have, we don't think that being put on a cloth mother has helped. We doubt if they do any better in infant relationships than if they were raised in isolation.

*Fremont-Smith:* Suppose you compare a cloth mother with a real mother, in terms of the babies' sexual behavior when they grow up?

*Harlow:* We don't have the data on babies with real mothers. We don't know whether the real mother is adequate to insure appropriate sexual behavior.*

Originally, we had raised our infant monkeys in single cages with a cloth diaper, and we often saw a strong attachment to the cloth. Figure 141 shows a 6-month-old monkey which we practically never saw. This response to cloth is similar to the attachment that human babies form for their teddy bears or pillows or rag dolls. We have also seen pictures of a baby gibbon showing this very strong clinging response.

Each day we took the diapers away for laundering and the baby monkeys would assume a distressed expression and sometimes even beat their heads on the wall. When we gave them back their diaper, they would put their thumbs in their mouths, the diaper against their faces, and close their eyes in utter ecstasy. We made a serious attempt to try to show that nursing is a variable of importance in the tie of the infant to the mother by having two cloth mothers, a brown one and a green one. This is a balanced design, but we will simply say that the green mother always nurses, and the brown mother never nurses.

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*At this point in his presentation, Dr. Harlow showed a moving picture to illustrate the behavior he had observed in infant monkeys raised on surrogate mothers.

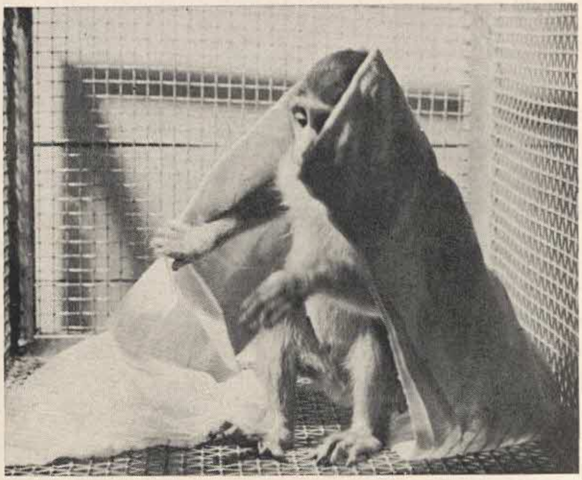

FIGURE 141. A 6-month-old monkey that has become attached to a piece of cloth.

Figure 142 shows the data. It can be seen that the baby monkeys develop an early preference for the nursing green mother, as if it were the sight of the green mother associated after feeding that produces a preference. This is a very interesting variable because it suddenly collapses as a variable of measurable importance somewhere around 80 to 90 days of age and never appears again, even though the monkey continues to nurse exclusively on the green mother. It is as if its nursing were no longer an unconditioned response.

*Reynolds:* The matter of the absolute color is not influencing it?

*Harlow:* No. There is no preference for brown versus green. Furthermore, in other tests, like the open-field tests, even before this period of time the mother which nursed the baby ceased to be a variable of importance, and it never returned. I think this shows very well that these factors must be traced ontogenetically in order to determine which variables are important. It is what variables are important when.

Figure 143 gives the data on the rocking crib versus the nonrocking crib. There is more individual variation here than with some of the other tests. Early in life, there develops a preference for the rocking plane as opposed to the stationary plane, but here again is a variable which collapses somewhere around 140 days of age, and from then on, there is no preference whatsoever. Perhaps it is because the animal himself has become so tremendously mobile by this time that he sup-

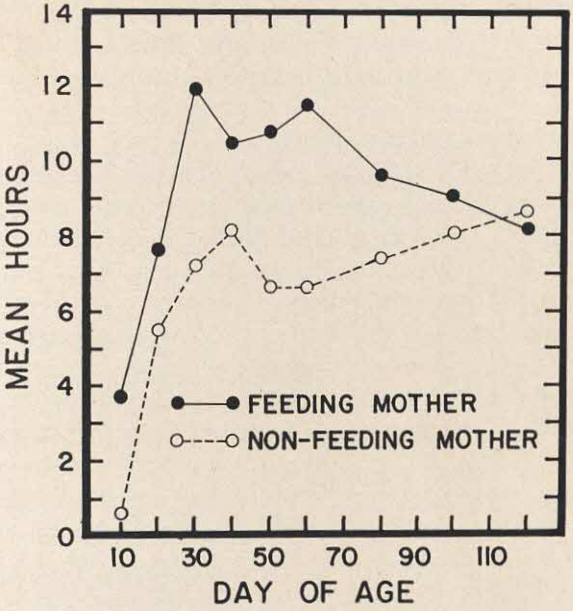

FIGURE 142. Time spent on differentially colored surrogate mothers.

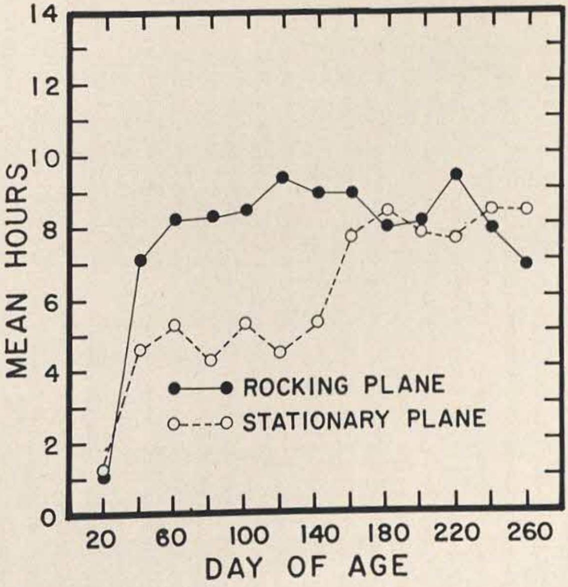

FIGURE 143. Time spent on rocking and stationary planes.

plies all the proprioceptive kinesthetic experience that is necessary. We think it is possible that some kind of motion, either artificial or initiated by the animal himself, is essential to the well-being of the animal early in life.

*Brazier:* Are these charts of single animals or averages of groups?

*Harlow:* These are averages of groups of four. We ordinarily work in groups of four animals. Shown here is a rocking mother versus a stationary mother. The same kind of phenomenon is present. It seems to be a reasonably stable phenomenon, although there is considerable day-to-day variation, and some animal-to-animal variation.

We pointed out the fact that our monkeys were quite steeply angled so the crib probably provided a better sleeping position. The animal could go either to a cloth mother or to a stationary plane. Early in life, there is a clear-cut preference for the plane. This preference collapses again around 120 days of age and there is a phenomenon of reversal; the animal now shows a clear-cut preference for the mother. Again, we think this is presumptive evidence that the ability to cling to the foreign form of the body, denied in the plane, is either a supportive variable or an independent variable in this affectional bond.

Figure 144 gives the objective data on the fear stimulus plotted the

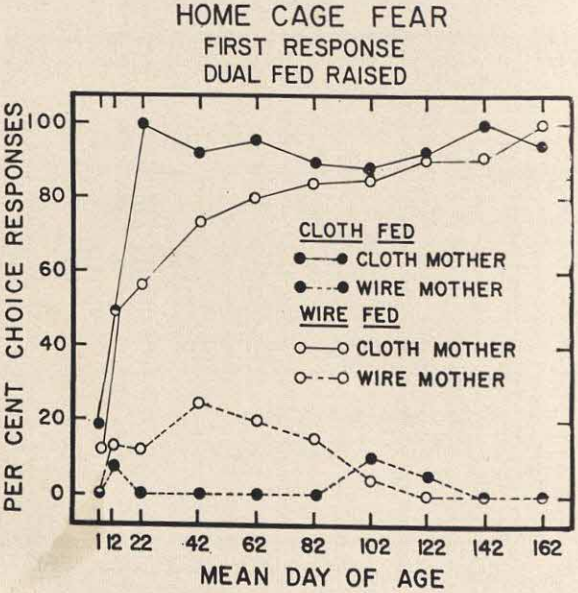

FIGURE 144. Responsiveness to cloth and wire surrogate mothers in home cage fear tests.

same way as for time on mothers. From the very beginning, there is a preference for the cloth mother, regardless of the nursing condition, but the almost 100 per cent incidence of going to the cloth mother doesn't come until somewhat later in life. Actually, the data plotted are somewhat more definitive than indicated. In this stage, the baby often runs blindly to the wire mother, then leaves the wire mother, and goes to the cloth. If he goes to the cloth mother, he stays there and does not go to the wire mother. This particular curve is of some interest. Early in life there is some increase in a tendency for infants fed on the wire mother to go to the wire mother, and then, even though these animals continue throughout all this period of time to nurse on the wire mother, this tendency disappears, and eventually there is, to all practical purposes, 100 per cent responsiveness to the cloth mother in the fear situation, regardless of the nursing condition which prevails.

Figure 145 shows the open-field test. We think—and I would like to emphasize this—that fairly early in the animal's life, the only thing he does is to cling, to attach himself. Then, subsequently, when he is older, the active contact with the mother gives him what we call security,

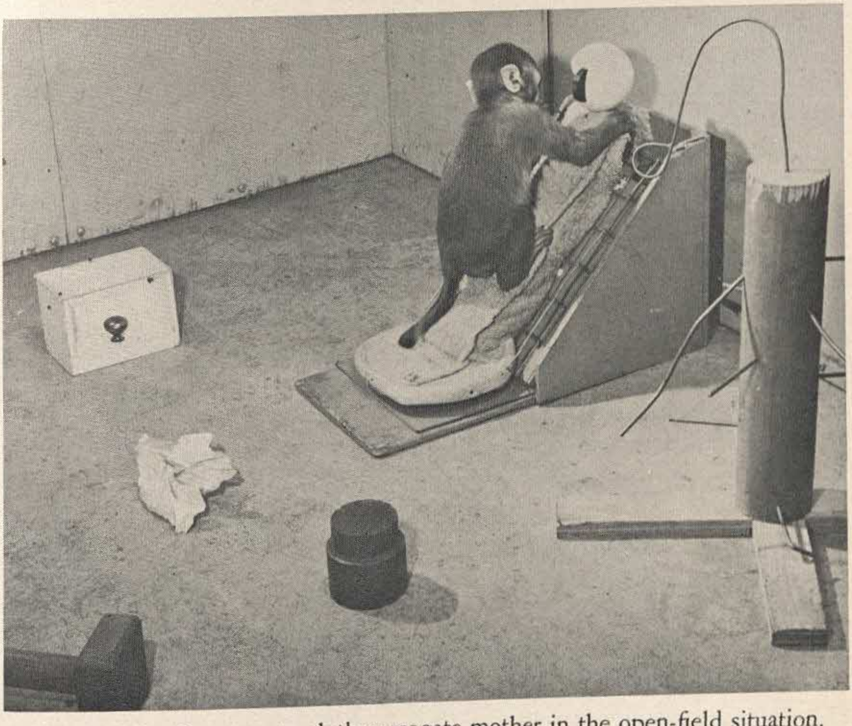

FIGURE 145. Response to cloth surrogate mother in the open-field situation.

so that he goes out and exercises all his potentialities as an exploratory, manipulatory animal.

*Bodian:* I notice in Figure 145 that the only object which could substitute for the shape of the mother is a cylindrical wooden tree, which you have prevented, by means of some projecting rods, from being used as a surrogate mother.

*Harlow:* Those projections are wonderful things.

*Bodian:* Perhaps for climbing but not for embracing. In the moving pictures, I noticed the monkey gave a passing glance at the cylindrical object, with its inhibitory projections, then went off and picked up the cloth.

*Harlow:* I don't think the animal will respond to a wooden mother as it does to a cloth mother, though I can't really say, as I have no data.

*Bodian:* I should think there would be a difference, because the wire is a discontinuous surface, and some of the monkeys, when the surrogate mother is removed in the fear situation, would rub up against the wall in preference to the wire, whereas the branch with the smooth surface and embraceable shape might have been preferred.

*Harlow:* I never thought of trying a wooden mother. A wooden mother might give an intermediate between cloth and hardware.

*Windle:* We found a great difference among young monkeys in the fear of objects. One fear-inducing object was a little iron horse; other objects created no fear but the moment this horse was shown, the monkey expressed fear. Have you observed that sort of thing?

*Harlow:* Monkeys, even baby monkeys, have a very marked preference for white over black. A black object can cause quite strong adversive types of response. Dr. William A. Mason* did quite a bit of work in trying to analyze stimuli that would call forth fear in the older animals. These tend to be large stimuli, brightly colored stimuli, particularly metallic and moving stimuli. He found, for example, that a snakelike form was no more terrifying than a nonsnakelike form, as long as size, mobility, and composition were controlled.

*Leese:* Dr. Harlow, you have shown us two or three examples of points in time when variables would drop out of the picture in the behavior of these animals, in terms of their preference. Is there any psychological maturation which you can see at that time in the nature of the animal? Is he more independent? Is he more self-asserting?

*Harlow:* I don't think we can answer that question. I think the young animals are becoming progressively more independent. We don't know when the play patterns in infants really come in and we don't know what their different forms are. We do know that play patterns are there by 150 days of age. Actually, we are sure that play patterns come in before 150 days of age, but at the present time we don't know exactly when.

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*Personal communication.

*Leese:* Professor Luria pointed out in his studies (6) on human babies that in the beginning of their language habits, he is able to pick out a point where there is a perception change and a time when they commence to develop an independence that I think he spoke of as parental separation. The youngster seems to be on his own now, so his behavior pattern has changed. This was around 2 years of age, or just over.

*Harlow:* As far as perception goes, we have observed animals which, for the first 10 days of life, climb up the feeding ramps and when they get to the top, they start to move their heads back and forth as if they could not see. Then, when the cheek contacts the nipple, they seize it and nurse. Around 8 or 10 days of age, often within a period of 24 hours, a very marked change in the behavior of these animals is seen. At 10 or 12 days of age, they are perceptive to form. At 20 days of age, our baby monkeys learn to discriminate a triangle from a circle as rapidly as they learn a black-white discrimination, with all the factors involved, giving presumptive evidence that form perception is probably innate in the monkey. Then, if you train them on circle-triangle discrimination and test for discrimination, everything is there, the whole adult capability to differentiate objects. This is at about 20 days of age. Color perception also comes in at about 20 days of age.

*Hess:* Shall we say: as tested by your tests, Dr. Harlow?

*Harlow:* Next, I shall discuss retention. We have a large number of retention tests in a wide variety of situations. The baby monkeys are kept on the cloth and wire mothers until they are 6 months of age. They are then separated from the mother and tested for the effects of immediate separation in out-of-home-cage-situations. They are then tested at 30-day intervals, one day each month being a test day, until they are 12 months old, when testing is done at 90-day intervals. Figure 146 shows, I think, very full retention of the response. In other words, once these affectional responses are formed, certainly in this mother-surrogate situation, retention is very clearly measurable at 18 months of age, and we are now beginning to get retention at 2 years of age and later, which holds up very well, at least on our better tests.

This kind of retention data for a response that is certainly in part learned is roughly comparable to that found for extreme fear or extreme phobia, which lasts a long time. I think it's good to know that affection

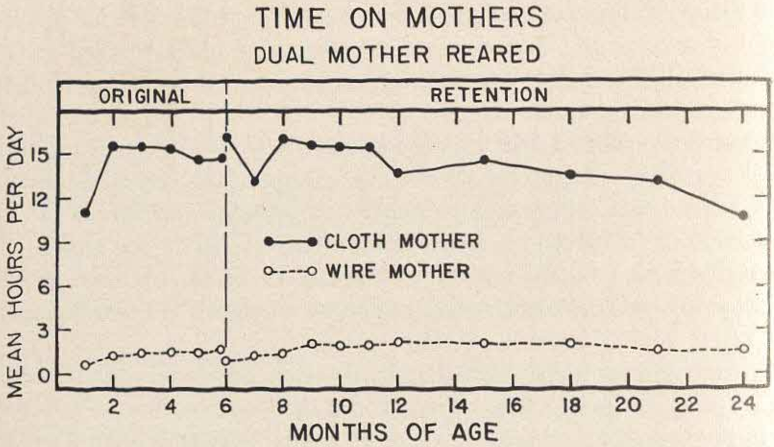

FIGURE 146. Retention of responsiveness to surrogate mother.

is a very persisting bond. But I am sure that nursing is not *the* variable which is producing this terrific affectional retention because its importance has gone out long before this time.

*Hess:* Do you have any figures on the responses of animals that have had no mother surrogate, in other words, that were not raised on either of these two objects?

*Harlow:* From birth on?

*Hess:* From birth on, or up to 6 months and then tested in the same way that you tested for retention in this series. Would they not perhaps make a similar choice in spending more time with the cloth mother than with the wire mother?

*Harlow:* We have the data.

*Fremont-Smith:* It's the question of what they would do if they were brought up on a live nursing mother. These are "dead" nursing mothers, in which you say nursing plays no role. In the case of a live nursing mother, in which she interacts, the nursing might play quite a role.

*Harlow:* That is a possibility. I don't see any reason why this can't be studied experimentally.

*Fremont-Smith:* I hope you will study this, because I think there is a tendency now to say that the nursing is playing no role, but the evidence applies only to nursing on an artificial, unresponsive mother.

*Harlow:* I'm willing to admit that the real mother is a very subtle animal. In the open-field test, a measure of contact-time shows that early retention is more than at 2 years. As the animals get older, and as you run them repetitively in the open-field test, there is a certain tendency for animals to adapt to it, and feel a good deal of freedom; so it has certain limitations as a retention test, but we think we have this matter under control now. Even so, a year and a half after separation, there is good indication of a strong preference for the cloth mother over the wire mother.

Figure 147 gives data on a group of animals that were kept in single cages until they were 250 days of age and then were put on the dual surrogate situation. In the first 48 hours, there was a good deal of fear for the highly ornamental face of the cloth mother. Then, after a period of time, the animals did attach to the cloth mother. Actually, they spent only half as much time on the cloth mother as do babies of the same age who have been on the cloth mother from birth. On retention tests, they frequently go to the cloth mother in the open field. Our observers found, on the objective records, that these animals don't seem to attach to the cloth mothers as do babies who have been there from birth. On the other hand, I think, even in this long delayed period of time, a reasonable attachment could still be formed to the cloth mothers. These infants were brought up simply on wire cages, with a cheesecloth

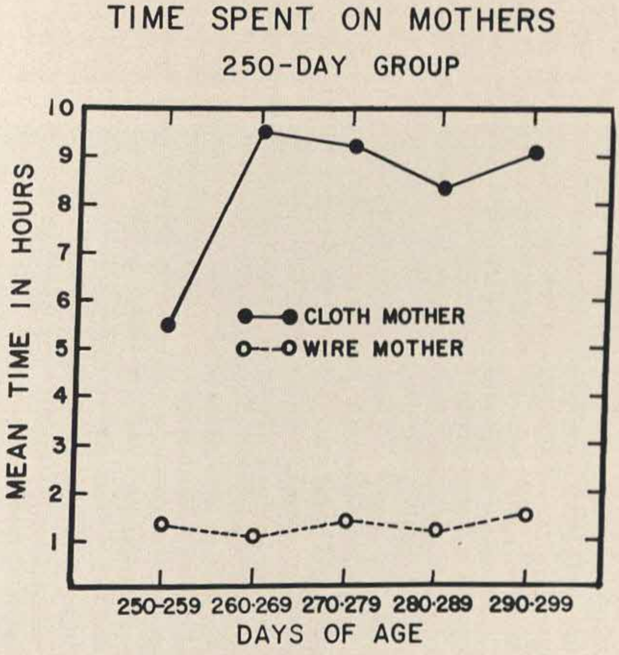

FIGURE 147. Responsiveness to cloth and wire surrogate mothers by monkeys placed in surrogate situation after 250 days of age.

pad, for the first 15 days, and then simply in wire cages, so they had no real mother and no surrogate mother experience whatsoever.

They climbed up wire ramps and when they got to the top, a bottle was there. Actually, the first six babies we had were fed by people, and we think they have shown a persisting responsiveness to people that is stronger than the reactions of animals who had only the most completely cursory and incidental contact with human beings.

Figure 148 shows our latest situation. It works out very well, either to measure affection or retention, because we have now put a fear stimulus into the open-field test. These fear stimuli are all toys. They are brightly colored, they move, and they make loud sounds. We so placed a Plexiglas shield that the monkey had to run around the fear stimulus if he wanted to make contact with the cloth mother. The animal was released from a start box, and all of the animals became very disturbed in this situation. In almost all cases, however, they did take the big adventure—they went around or jumped over the Plexiglas and reached the mother. We used different kinds of mothers, sometimes both the conventional wire and cloth pairs of mothers, sometimes one or the other. When the animal gets to the mother, it clings to her and relaxes.

*Fremont-Smith:* Might not a real mother give a signal to the infant in one way or another that would indicate real fear, and might not the

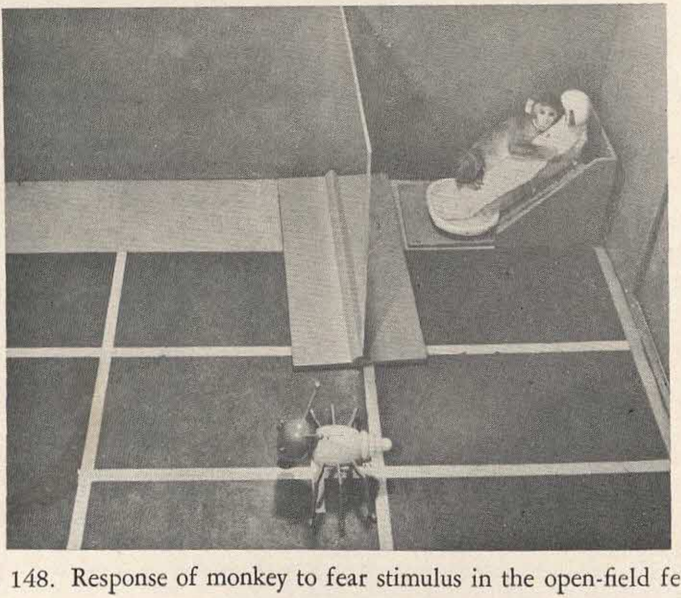

FIGURE 148. Response of monkey to fear stimulus in the open-field fear test.

absence of such a signal or the placidity of the mother, which would be certainly present in the nonliving mother, be a signal reassuring the baby that, after all, there was nothing to fear? Perhaps in real life there is an interaction process in which the baby runs to the mother to find out whether the mother is also frightened.

*Harlow:* Babies sometimes get away from the real mother, and if a stranger approaches and the baby runs back to the mother, the mother then automatically threatens. To our surprise, we can see no indication that the babies learn or show any sign of learning to fear the person because of this maternal behavior.

*Fremont-Smith:* There would be no difference whether they ran to a real mother that did nothing or to one that threatened?

*Harlow:* It doesn't seem to make any difference to the baby's responsiveness, as far as we can see.

*Fremont-Smith:* How long would it take for the infant to relax? Wouldn't it take much longer when it went to the inert mother than when it went to a real mother that threatened?

*Harlow:* It is very hard to say, because it goes to the real mother and it may cling or just stand in the mother's arms. It's hard to measure this sort of behavior.

*Fremont-Smith:* But you can tell when it began to relax, when it would show its curiosity. This could be measured.

*Windle:* A baby monkey won't go to another's mother if she threatens. When it accidentally gets too close, the adult may injure it severely.

*Fremont-Smith:* But the contrast here was between its own mother, which is a real mother, and an inert, artificial mother.

*Harlow:* If the baby is away from the mother and a stranger approaches, the mother has a particular sound to which the infant responds. I don't know whether that is a reflex response or not. Figure 149 is a very dramatic illustration. This is a baby monkey that 2 minutes before was showing signs of abject terror. It went to the mother and rubbed against the body of the mother or as we say, it "rubbed in mother love." Then, just 120 seconds later, it went out, not only to explore this world, but actually to explore this stimulus which had just caused such terror. We have had three cases of baby monkeys in this situation which first went to the mother and then tore the toys to pieces, shredded them. This is what one would call security, when they will go out and attack these objects that otherwise leave them in a state of utter collapse.

*Bodian:* May I ask whether you removed the surrogate mother after

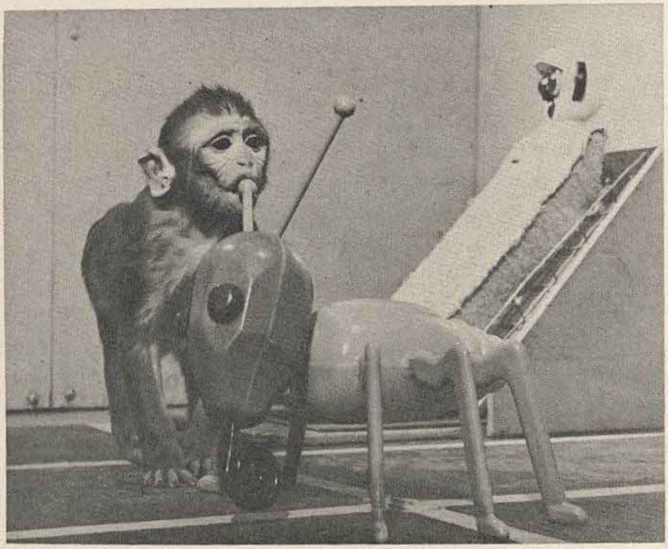

FIGURE 149. Monkey exploring fear stimulus in open-field fear test.

they had "rubbed in mother love?" Does that make any difference?

*Harlow:* I am sure they would collapse. We have never done it. The act of contact is necessary, but I'm sure the mother has to be present, visually at least.

*Bodian:* What about a Plexiglas-shielded mother; can she produce the effect of security?

*Harlow:* Yes. But statistically, they are not as free in the open field when the mother is shielded, even though they have had considerable experience with the shielded mother.

*Bodian:* What I'm trying to learn is whether the infants must do the rubbing, or whether it is the presence of the mother that counts?

*Harlow:* If they cannot make contact, there is not as complete a picture, no matter what. But there is no question; the actual sight of the mother is important.

*Fremont-Smith:* And they rub against the Plexiglas shield, don't they?

*Harlow:* Yes, that's correct.

*Fremont-Smith:* So they have substitute rubbing.

*Brazier:* When the little monkey pulls the toy apart, does he appear to be attacking it aggressively to destroy it, or is he picking it to bits out of curiosity?

*Harlow:* I think, in these cases, it looks more like aggression, although, perhaps, it is just manipulation. These animals are fairly destructive, and these look like aggressive attacks.

*Windle:* I would like to mention the incident of a female monkey which was kept with her real mother for more than a year. The mother would not allow her to eat, but kept her at the breast. Presumably, all the food that she received was from the breast. These were monkeys in another laboratory, which were offered to us because it was thought the baby might have cerebral palsy. We took the mother and baby, and found that the baby had an advanced case of rickets. I understand that monkeys don't usually live that long when they are severely rachitic. Needless to say, we took her away from the mother and began to feed her. She is now over 3 years old, is stunted, and is beginning to menstruate.

*Harlow:* We have some interesting observational data on these retention tests. By the time the baby is 2 years of age, he is twice as big as his mother surrogate. When put under retention test, in a 6-foot room with the mother surrogate, some of the babies pick up the cloth mother, hold it tenderly to their breast, and walk around the room, holding this mother surrogate, as though feeling secure.

*Bodian:* Did you ever see a child with a doll?

*Harlow:* It's the same thing. Our study of baby monkeys has led us to believe in an imitation reflex which is one of the strongest reflexes we have observed. When one baby goes to one place and then leaves, another baby goes to the same place. One baby goes to a particular inanimate object, and the other goes to the same inanimate object. We think this is a reflex that can be found in the first 10 to 15 days of age.

*Fremont-Smith:* Reflex imitation? But you're calling everything that a baby does in the first few days a reflex. Is there anything the baby does in the first 15 days that you don't call a reflex?

*Harlow:* Yes. If the baby of 15 days of age or less is put in a learning situation, he learns. We then call that learning. I think that learning takes place from day 1 on, and in these late patterns, it is impossible to unravel the learned from the unlearned components. The only thing we are trying to say is that we think there is a large unlearned component in these quite complex patterns of behavior.

*Fremont-Smith:* I was hoping that you would put quotation marks around "reflex."

*Harlow:* The only thing I am struck by is this: that very early in life when the mother orients, the baby orients. When the mother reaches, the baby attempts to reach. When he gets away from the mother, he goes and explores. In the case of food, if we raise our babies on surrogate mothers in isolation, we have a hard time to get them to make the transition from liquid to solid food. We can usually do it in 15 days, but it is really a struggle. In the case of young infants, when an apple is placed in the mother's cage, the mother will eat it, dropping a few shreds. The baby will then pick up the pieces and put them into his mouth. Sometimes babies of 20 days of age ingest apples, and sometimes the greedy mother pries the baby's mouth open and takes out the food. I often thought that if human mothers would raise their children that way we would have fewer feeding problems. Some of these babies form an appetite for food very early. We can then use solid food to lure the baby from the maternal chamber into the observational chamber through a doorway too small for the mother to follow. We hope that this matter of appetite will prove to be consistent, because it could be an extremely useful thing in the study of infant-infant interaction.

*Fremont-Smith:* You wouldn't call that a reflex, then? That is learning?

*Harlow:* I think putting food into the mouth is learning. I don't want to be an iconoclast, but I am very skeptical that there is any fundamental difference between maturation and the process of learning. I don't think it is anything we can really answer. It is a very hard thing to discuss technically, but these are phenomena that may have more in common than they have apart, and simply produce different kinds of external stimulation. Learning had to come out of some place.

Figure 150 shows two baby monkeys living together. As Van Wagenen (9) said, you must never put newborn monkeys together because they may literally smother each other. This picture, however, is at 90 days of age. This is what we call the "together-together" situation; these babies are literally wrapped together. We are now testing them on infant-infant affectional responses, both here and with two other babies. Our first thought was that they would never be able to break this clasping pattern at all, that this was a kind of early experience that would make it impossible for them to adapt to normal infant-infant interactions. We don't know if this is true, but, certainly, this particular pattern is an example of an early fixation that ordinarily is not seen.

*Reynolds:* How does an infant suffice as a surrogate mother? Or am I anticipating?

*Harlow:* I think both of these infants are surrogate mothers, mutually tied to each other. These animals are raised together, in a relatively small cage, so that they have maximal opportunity to develop this kind of responsiveness. Once formed, it is extremely persisting. These animals are now close to 200 days of age, and they are just beginning

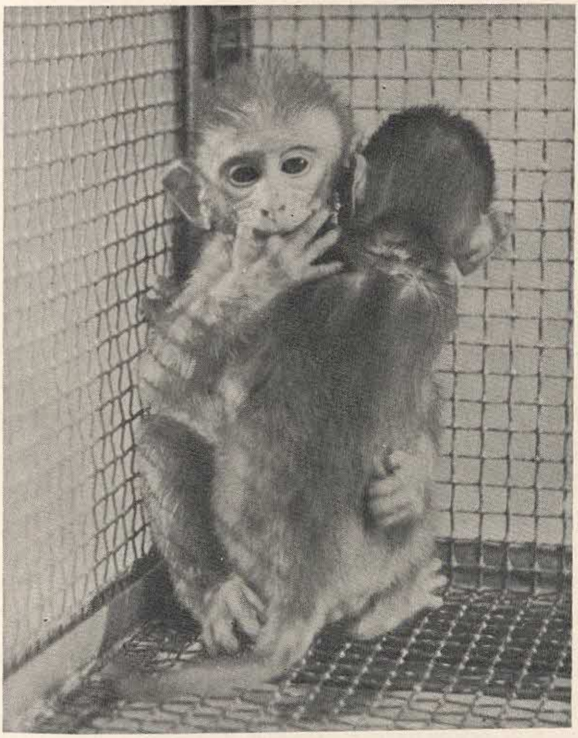

FIGURE 150. Typical behavior of two monkeys reared together after day 90.

to become independent in a test situation. Whether they are ever really going to break away from each other, I don't know.

*Fremont-Smith:* Do monkeys ever have twins?

*Windle:* Yes, they do have twins, in the same proportion as man. Twins do occur in nature. Furthermore, a mother will adopt a second infant, if she can steal him.

*Bodian:* We have seen such clinging in the cage, for well over a year, in monkeys which had been about a year and a half old when they first arrived. Once they attach to another receptive juvenile, they may hang on for dear life for at least a year.

*Harlow:* We have attempted to produce experimental neuroses. Since our infants have this long-time maternal attachment, it should offer unusual opportunities to create experimental neuroses. We don't know how successful we have been with this. One technique we have tried is to have a wire frame over a spun nylon cloth mother which rejects, but this doesn't seem to be working out too well. Another surrogate mother has a series of nozzles coming down the ventral surface of the body, and these nozzles are air squirts. An air blast is a very adversive stimulus to the monkey, on a preventive reinforcement basis. We have put two babies on these mothers from birth. They do not leap away from the air blast, but cling tighter. The animal, faced with an adversive stimulus, responds by holding tighter and tighter, taking the air blast.

These babies, in the open-field test, show no affection for their mothers. Actually, these animals appear to eat an inadequate, or less than normal, amount of milk, and they seem to show weight deficits. Furthermore, they have been tested in social situations and, up to the present time at least, they appear to be failing to make any kind of adequate infant-infant relationship. Perhaps we have created very seriously disturbed babies by this technique.

We have attempted to vary the rearing situation by using two babies, each raised on a cloth mother, who can make contact through the bars with each other (Figure 151). After 180 days of this situation, we tested them to see if they would be more adequate in forming social relationships than babies who have been raised alone on surrogate mothers from birth. We really don't know how successful we have been in this situation. If these infants are put in the open-field test with no surrogate mother, they seem to derive a very considerable amount of security from contact with each other. In a fear situation, however, they will always run to the mother for support as I think would be expected.

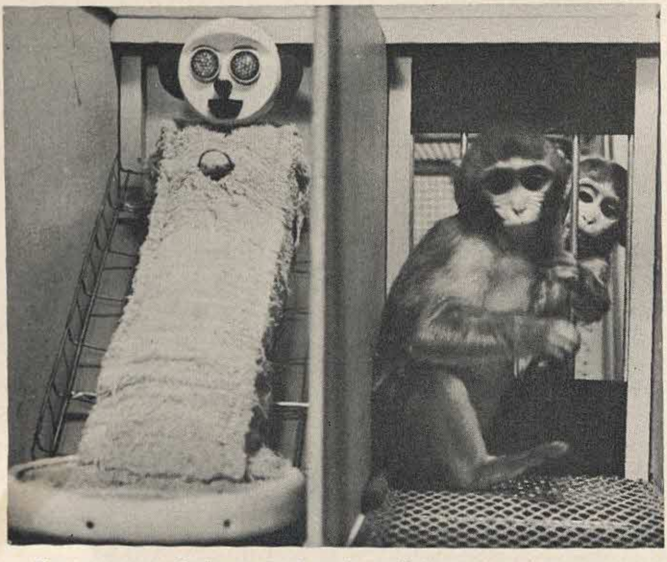

FIGURE 151. Infant monkey in social-surrogate situation.

In the home cage, the babies spend most of the time on the cloth mothers, making little physical contact with each other. You do see signs of their responding to each other in, perhaps, simulated observation or play.

*Fremont-Smith:* In the field situation, where there is no mother, do they cling to each other?

*Harlow:* Yes, but if a mother is put in, they abandon each other. If infants that have had only relatively casual experience with human beings are put in this 6-foot cube room and a person also put in, they go to the person instead of to any inanimate object. We have two baby monkeys who, from birth on, were raised in complete isolation; that is, they were in an illuminated chamber, but they never saw or had any apparent meaningful auditory associations either with human beings or other monkeys. At the same time, it was possible to test their learning capacity by remote control. These babies, in complete social isolation, ate and drank a normal amount of food, gained a normal amount of weight, and were physically completely healthy. At the end of 2 years' time, they were taken out of this situation and tested both together and with other monkeys, and they were completely lost socially. They would just sit. A little animal half their size would come up and start to explore them. Getting no response, he would push them, pull their hair, and bite them, but all they would do would be to turn their back and walk away a little, sit down, and wait to be abused again. These animals are now being tested 18 months later, and they still seem to show a great deal of social inadequacy. They still allow other animals to abuse them, making no effort to fight back, and they often make rather inadequate efforts to escape.

Figure 152 shows a technique which we think shows real promise for the effective study of infant-infant interaction. In this, our "playroom," we put very young babies, 10 days of age or less, and they show no clinging responses. Even though they touch each other, the clinging response is not elicited. As a matter of fact, they don't show any play responses at first. We have a number of duplications in objects here because we are very much interested in studying the kind of imitative behavior, whether or not it is reflex, which seems to come in extremely early, and to persist from then on throughout the animal's life span. It was on this ladder that the poor animal I spoke of earlier got fixated to the rung.

We are quite convinced that if you want to study infant-infant interaction, you shouldn't put the babies in a featureless room. They must be in a place where they will be stimulated. We are quite convinced that

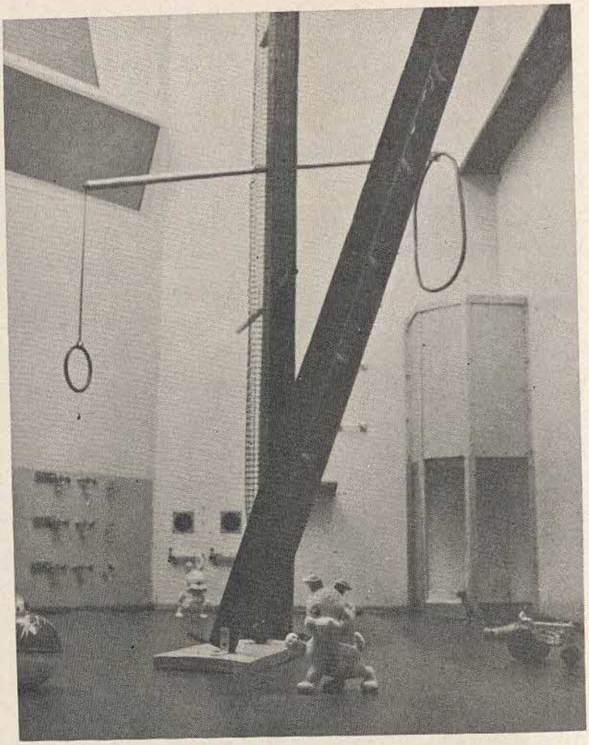

FIGURE 152. The playroom test situation.

the infant-infant reaction arises out of inanimate object exploration, and then, at appropriate maturational ages, the animals find that the animate object is a better plaything than the inanimate, so perhaps they mature very specifically, in highly mature play patterns.

*Reynolds:* They don't show any fear response to this?

*Harlow:* If you start them early in life, before the fear responses mature, they are never going to show any fear of this, just as when you attach them to a fearful face, they never show any fear, either.

Figure 153 is a schematic diagram of the kind of situation that we are going to use with both the real mothers and the surrogate mothers. In each of these chambers, there is either a real or a surrogate mother and a small door, large enough so that the baby can come and go as it wishes, but too small for the mother to follow. In between the living cages are the test chambers in which objects such as playthings, exploratory devices, or pieces of food can be placed. Early in life, the interactions between two babies will be studied, and later all four infants will be brought together since four animals seem to be a very good

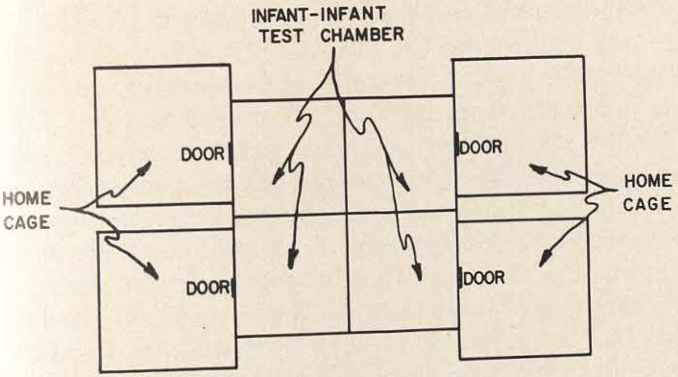

FIGURE 153. Diagram of multiple mother-infant living situation.

number of animals to elicit a maximum amount of play behavior and still give an opportunity to trained observers to keep adequate records on them. In this, we will make our first attempt to compare directly babies raised on real mothers and surrogate mothers.

By the way, if the prefrontal areas of cortex of the baby are taken out bilaterally, neither its affectional responses to other babies are interfered with nor its responses to a surrogate mother. If phenylpyruvic oligophrenia is induced in baby monkeys by appropriate diets from birth onward, this does not affect their reactions to the mother. The reaction to the mother is a really strong response. You can produce quite a range of cerebral insults, without destroying it.

We are very interested as to where the centers that will control the affectional response are in the brain. We hope sometime to unravel these.

*Hess:* I feel that Dr. Harlow should be particularly commended for dealing with a complex problem of behavior involving a complex animal and then obtaining quantitatively useful and important data. Certainly we all will benefit from the results, particularly since they provide us with comparative material in the general area of maternal-child relationships and in the maturational sequence of various other behaviors. One suggestion I would like to see carried out some time is to determine whether the administration of meprobamate would also inhibit the formation of mother-child bonds as has been shown by us with fowl. In those experiments, the association effect was lost when experience with the surrogate mother took place under the influence of this drug.

I would like to ask a question or two which, I think, might clarify something for me, and perhaps it will for some others also. The first relates to the monkeys that are raised on two differently colored surrogate mothers. The graph shows a general trend of no appreciable difference in responsiveness at about 100 or so days of age. I would like to say that this might seem to indicate that the monkey is not making a discrimination, whereas, in actuality, the experimental situation set up in another way might show an extreme differentiation, that is, if the animal were raised exclusively on one colored parent object, up to a certain period of time, and then, at that particular point, tested for retention, as you did with some of the wire and cloth mother objects. I say this only because I feel that factors such as light colors and different kinds of heads might be very important in determining, in the studies you are planning to do, whether or not individual recognition takes place. Actually, that wasn't so much a question as it was a comment, but I would be happy to have you say something about it.

*Harlow:* As we know, of course, animals must perceive the differences in these mothers, because they can perceive infinitely more subtle differences in stimuli. I think your point is well taken, that there may be techniques by which you can show that this is possible, by fixating them on a single nursing mother, although it wasn't successful with the wire mother. With the cloth mother, you might be able to produce this kind of situation.

*Hess:* I particularly raise the point because we have found, in working with fowl, that if a baby mallard or some other subject is allowed to be taken care of by only one individual, one person, for as little as a week or two, this animal will not go to any other person. But if two or three people are used—because, after all, one doesn't have that much time to spend on the animal and so have to take turns with somebody else to take care of it—this is enough for it to generalize its behavior to all other individuals and it will go to anybody, not just these two or three.

The phenomenon that Dr. Harlow observes with the two colored objects would, therefore, be for me quite reasonable to expect, even with the difference in experimental animals with which we work and with which he works.

*Harlow:* A baby raised with a real mother and then allowed to go out and explore the cloth mother shows interest in the cloth mother. Whether it would, if you separated it from the real mother, is an open question.

*Hess:* The next point is that you described something that I did not know existed in baby monkeys, and, again, it reminds me of the situation with ducks. That was your description of the monkey following a towel when it was pulled. Does this always happen?

*Harlow:* This is an unreliable response; at least, we haven't been able to produce it reliably, so we have some worry about it.

*Magoun:* Do not chronically decorticate cats show this following response to an unusual degree, so that they follow any moving object, wherever it goes?

*Livingston:* Yes, and also septal and anterior thalamic ablated cats according to Bond and his co-workers (1).

*Magoun:* This suggests that the mechanisms involved here may not depend upon the cortex, in that they seem, if anything, to be exaggerated after decortication in the adult animal.

*Harlow:* A casual observation by Heinrich Klüver was to the effect that a monkey which had been a very good mother failed, following deep bilateral temporal transection, to show any maternal behavior whatsoever after two subsequent pregnancies. Dr. Earl Walker has made a casual comment that following bilateral amygdaloidectomy, a monkey that became a mother failed to show maternal behavior. This seems entirely possible to me. We are going to make an attempt to unravel some of these affectional systems. As a first guess, I would make the assumption that these patterns are controlled by rhinencephalic structures.

*Pribram:* This has not held up completely in all cases, however. Maternal behavior does occur after hippocampectomy or after cingulectomy.

*Fremont-Smith:* In what species?

*Pribram:* Rhesus monkey, and also baboon. When I said "maternal behavior," I think I should be more specific, because Stamm (8) has shown cingulectomy affects maternal behavior: the retrieval of infants into the nest. What I was referring to with respect to rhesus monkeys and baboons is whether they will be protective of their young in a family situation.

*Erikson:* My problem is simply this: I think in a clinical framework and in the framework of the life history, while most of you have done experiments and can talk to each other about research planning and experimental design. Konrad Lorenz once said in a meeting that the people who understand each other best are those who have moved logs together. You have moved logs together, and I envy you the ease of your communication. It fascinates me, I think I am learning, but the rethinking in terms of my own work takes more time than fits into your tempo of communication.

The problem is something like this: Take a face, or, rather, an oval or circular surface with two points in it. The human child smiles at it, a bird is frightened by it. You see the sensory and neurological unity of these two events. To me, they are from two different worlds. When the infant smiles at what looks like a face with two eyes, there is a certain history behind it, somebody has smiled at him, and looked at him while doing things for or to him. In front of him is a whole long life history in which intricate values associated with the human face will gradually develop out of those first cognitive steps that you isolated.

I would also think of aspects of the total situation which you ignore when isolating what you are after: for example, what role the mother's voice plays in this; was the bird in a nest when he was caught? Did the mother bird act frightened whenever anything like an owl appeared?

I can't help wondering, then, what variables are important at which stage of life, each life-stage occupying, of course such a different place in the totality of the child's and the animal's life cycle. Two such similar situations are for me so different that it will take me days to think about them. I, therefore, have to ask your indulgence, and ask you to believe me when I say that I am extremely appreciative of everything you are demonstrating.

When it comes to the monkeys, things get a bit worse, particularly because Dr. Harlow, in a way which is admittedly humorous and analogistic, uses such phrases as mother-love in connection with experiments which in themselves, of course, are most ingenious. Maybe I am a sentimental clinician who cannot accept the idea of calling a wire cage a mother. But I cannot help thinking that there is probably something scientifically wrong in this nomenclature. To my mind, all the functions of a mother animal in the life of a monkey are here taken care of by human beings. What the experiment isolates is only a part of what humans do for the monkey and to it; all of which is now his "habitat." If the infant monkey makes a partial and specific attachment to a wire figure, which is described as "the animal, in climbing on the cloth mother, rubs the mother love into itself," I feel that there is something not quite right. I would assume, for example, that the cloth doll smells of the people who handle the monkey and give him affection, as was so clearly indicated in Dr. Harlow's way of speaking about it—people, incidentally, who are clothed in cloth. Then, it is more than an attachment to that cloth doll as a substitute of the lost (and never known) mother: the attachment includes a fixation on those who put the cloth doll there. I am merely explaining again why I would have to ask and think much more about this before I could say anything. I can't deny, for example (and I have seen Dr. Harlow's moving picture twice now), that, to me, these are experiments in creating fetishism in monkeys; which shows, to me, clinically, that because monkeys are closer to us than other animals are, we can create substitutions in their affectional diets; but what goes with it is also the facsimile of a human neurosis. This, in itself, is, of course, a great field for research, and Dr. Harlow's demonstration is fascinating.

*Hess:* I have a short film* that is quite relevant to what Dr. Harlow has been showing in monkeys. One can compare the kind of responses made by infant monkeys to mother surrogates with the kind of responses that young mallards make to their mother surrogates, which are actually replicates of mallards.

I think I can tell you, in just a few moments, something about the actual experimental procedure. The young mallards come out of eggs which are incubated and hatched in a dark room. At the time of hatching they are placed in small individual boxes.

At about 15 or 16 hours after hatching (which we found to be the maximally effective period for this kind of learning in mallards and which we have been talking about as "imprinting" since Konrad Lorenz coined that name), we merely place them on a circular runway that has plastic walls, and expose them to a male mallard decoy. This will be the surrogate mother, or substitute mother, or, as we generally refer to it, the imprinting object. The only visual experience that the young mallard has when it is placed for the first time in a visual environment is this object which moves, suspended, around the runway. From a loudspeaker inside the model, we produce a continuous sound which is "gock-gock-gock-a-gock" from a tape recording.

*Reynolds:* Is that a recording of a real female duck?

*Hess:* No, it's just a man saying exactly what I have said. That is the experience that they have. They make four turns around; that is, a 12.5-foot circumference, so they have followed this object for about 50 feet. Then they are removed from the situation, placed back into a cardboard box, and later we test to see whether they go to this object, which is a male mallard decoy and has a green head and a white band around the neck, and is different only in coloring from the female mallard, which is our test object.

In our test situation, what I want to show you is not our laboratory procedure. Occasionally, we do what I call field studies, just to satisfy ourselves that what we are doing has some relevance to the way the world works and isn't just an artificial laboratory situation.

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*Dr. Hess showed a moving picture, the contents of which are discussed in the text.

We go down to the duck pond, and here is a situation where the actual mother is present as a stimulus which might attract them more than this object with which they have had experience for so short a time.

In the film, is a male decoy with two young mallards that have been imprinted on it. We merely pull it by a string in the water. I would like to stress particularly the behavior that occurs at that time, and also what happens when the real mother comes in to try to lure the young mallards away. The mothers with new young try to get other young to come to them.

Then, after that has happened, we lift the decoy out of the water with the string, so that now these two imprinted young mallards don't have any "mother" available. But, at the same time, we start the gock-gock-gock sound in the male decoy, which is now sitting on the edge of the pond, and next to it is a female mallard decoy with its proper brown coloring and with the sound of a real female calling her young playing through the loudspeaker. The real female is also present but in the water. We release a third young imprinted duckling who has been imprinted on the male model. This young imprinted duckling makes a choice of the male decoy. Subsequently, the live mother will also come into the picture, with her two young, again trying to lure the imprinted ducklings away.

*Reynolds:* Are these wild mallards?

*Hess:* Yes, wild mallards, as wild as we can get them. Konrad Lorenz insists they are not wild. He says he can tell by looking at them. I tell him I have no definition of wild mallards except that these are the mallards the hunters shoot at in the Chesapeake Bay area, and, to me, they are wild. When the decoy is pulled away, the young swim after the model much in the same way that young actually follow their real mother.

*Pribram:* Do you observe any separation anxiety?

*Hess:* Let me say this first. When the real mother comes in, not only do they avoid her, but they actually go to the far side of the decoy and secondarily get quite close to the decoy. I thought this particularly interesting, because it appears to me to be quite similar to the young monkey's behavior when it is placed in that kind of situation.

*Windle:* Does the decoy quack?

*Hess:* No, there is no sound because it is just a floating model. They follow it by its visual aspect alone.

The young duck in the film first went to the wrong decoy, but he immediately corrected himself, and then made little conversational sounds to the model, which is similar to the one on which he had been imprinted. The other two ducklings apparently heard the sound, and came steaming around to go to the model which is making this sound.

*Reynolds:* Meanwhile, the female decoy is making a sound?

*Hess:* She is making a quacking sound, the way a normal female would, calling her young. While the ducklings occasionally get quite close to the male decoy, they also will go off and play in the water, dive in the water, and so on. But under conditions where there is a real danger, you will often see them go very close to the decoy. When we drive the female away and make other threatening sounds—in fact, we throw some pebbles at her—what happens is that the three that were imprinted so briefly on the male decoy end up by going to the male decoy, and the female's own ducklings, of course, go and join her.

This is the kind of behavior they engage in. They often will just sit near the decoy in the sun. They will also preen themselves in the area. But, on the whole, their behavior is reasonably similar to that which the young will carry out in relation to their own mother.

*Reynolds:* Are these ducks fed by their mother?

*Hess:* No. Ducks do not feed their young. They may lead their young to food, but do not actually feed them. This particular film has relevance in that it is possible to compare with Dr. Harlow's monkeys a completely different species, which does have learning of the parent object and which shows preferences for one kind of parent over another, when you allow the animal to make a choice. It shows in other instances the kind of social attachment and other behaviors that, in some degree, seem to me to be quite universal, at least in some of the other animals in which we have looked for it. We have also looked at this maternal-child relationship in the lamb, which has been studied by several others to a larger degree. We have also worked with the guinea pig, and there seem to be certain quite similar processes. I thought it might be interesting to compare this behavior, which is characteristic of animals that are immediately mobile at birth and are reasonably self-sufficient, with the much more helpless situation characterized by the monkey.

*Bodian:* One of the things that seemed to me to be rather interesting was the fact that in the case of the duck, the stimulus was purely visual, whereas, in the case of the monkey, I'm not clear whether there is a single sensory component or whether it is a mixed component, whether it is tactile plus visual or tactile plus kinesthetic. Have you thought much about the problem of whether there is a single critical element in this, with the other playing a minor role, or whether you need two? This might determine your first approach to ablational studies. If there is a critical sensory component, one ought to be able to discover it first by means of observations of behavior, and, second, by careful ablation studies.

*Hess:* I want to hasten to add that since I did not go into the details of the imprinting experiments with the waterfowl, you couldn't know that actually we find auditory, visual, and tactile cues all to be of importance. In fact, temperature can also be a factor.

*Fremont-Smith:* Will they operate separately?

*Hess:* You can work with each of them quite separately; in fact, one can imprint the animals to a moving sound, with no object being seen. One can do this by running the loudspeaker under the runway. It can be shown that contact alone will produce this conversational tone response. By working with a decoy in the dark, every time the animal is touched, it makes those little responses and tries to keep up with it. But the combinations just work better, ordinarily, than any one of the components alone.

*Bodian:* Are all these equally powerful when used singly?

*Hess:* No. the visual stimulus is better by itself than the auditory, although I cannot give you quantitative measurements, except that a larger percentage of animals follows the visual object than a moving sound, but a much larger percentage follows a moving sounding object than a moving silent object, and so on. On this, we have quite good figures.

*Magoun:* Each of these modalities seemingly is equally potential in evoking activity in the limbic mechanism, so I question whether a study of afferent discrimination will be very helpful to you.

*Livingston:* There is a possibility here, perhaps, in relation to Dr. MacLean's theory that the amygdala is related to preservation of the self, and the septal region of the limbic system to preservation of the species (7). I wonder whether the maternal behavior might be more closely linked to the anterior part of the limbic system.

*Pribram:* The septal region, you mean? I don't think that has been checked, at least not in the monkey. It may have been done in the rat.

*Purpura:* As I understand it, visual cues play a decisive role in the imprinting processes in Dr. Hess's experiments and, of course, Dr. Harlow's monkeys utilize tactile cues in addition to the visual. Are there any data available for an animal such as the cat, which does not rely on visual cues? In other words, what are the major factors involved in imprinting in an animal with delayed eye-opening? The newborn cat is more immature than the newly hatched duck or newborn monkey. The developmental stage of the cat at birth is similar to that of the newborn human infant.

*Hinde:* T. C. Schneirla and J. S. Rosenblatt at the American Museum of Natural History have made a very detailed study on cats.* I think olfactory, tactile, and kinesthetic senses all come in. The young not only find their mother but they will also find the same nipple, and become attached to one particular nipple.

*Keller:* I was going to say that I suspect that among cats, as well as among sheep, the mother pays considerably more attention to the young than hens do. For instance, if you want to have an orphan lamb put onto a mother that has lost a lamb, you must skin the dead lamb and put the skin over the orphan lamb in order to get the mother to accept it.

*Hess:* Although you can get the same result by putting her own milk over the to-be-adopted sheep.

*Keller:* Yes, that's right.

*Fremont-Smith:* It's the olfaction you have to deal with.

*Keller:* Yes. But there you have the mother coming to accept the young more than you do here. The more helpless the young, the more helpful the mother, and also in certain species more so than in others, I would say.

*Magoun:* May I make a brief statement in this field of imprinting, which your mention of the sheep called to mind? In Charles Darwin's voyage to South America, a century ago, on the Voyage of the Beagle, he was impressed with the role of the sheep dogs in guarding the flocks. He learned that at birth the pup was taken away from its mother, put with the sheep, nursed at a sheep, and kept entirely away from the other dogs until he had matured; then he was castrated so that he would not later develop a sexual interest in other dogs. I think that this must be one of the early descriptions of imprinting, and it is not in the technical literature. These are Darwin's words from his *Voyage of the Beagle*:

"While staying at this estancia, I was amused with what I saw and heard of the shepherd-dogs of the country. When riding, it is a common thing to meet a large flock of sheep guarded by one or two dogs, at the distance of some miles from any house or man. I often wondered how so firm a friendship had been established. The method of education consists in separating the puppy, while very young, from the bitch, and in accustoming it to its future companions. An ewe is held three or four times a day for the little thing to suck, and a nest of wool is made for it in the sheep-pen; at no time is it allowed to associate with other dogs, or with the children of the family. The puppy is, moreover, generally

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*In preparation.

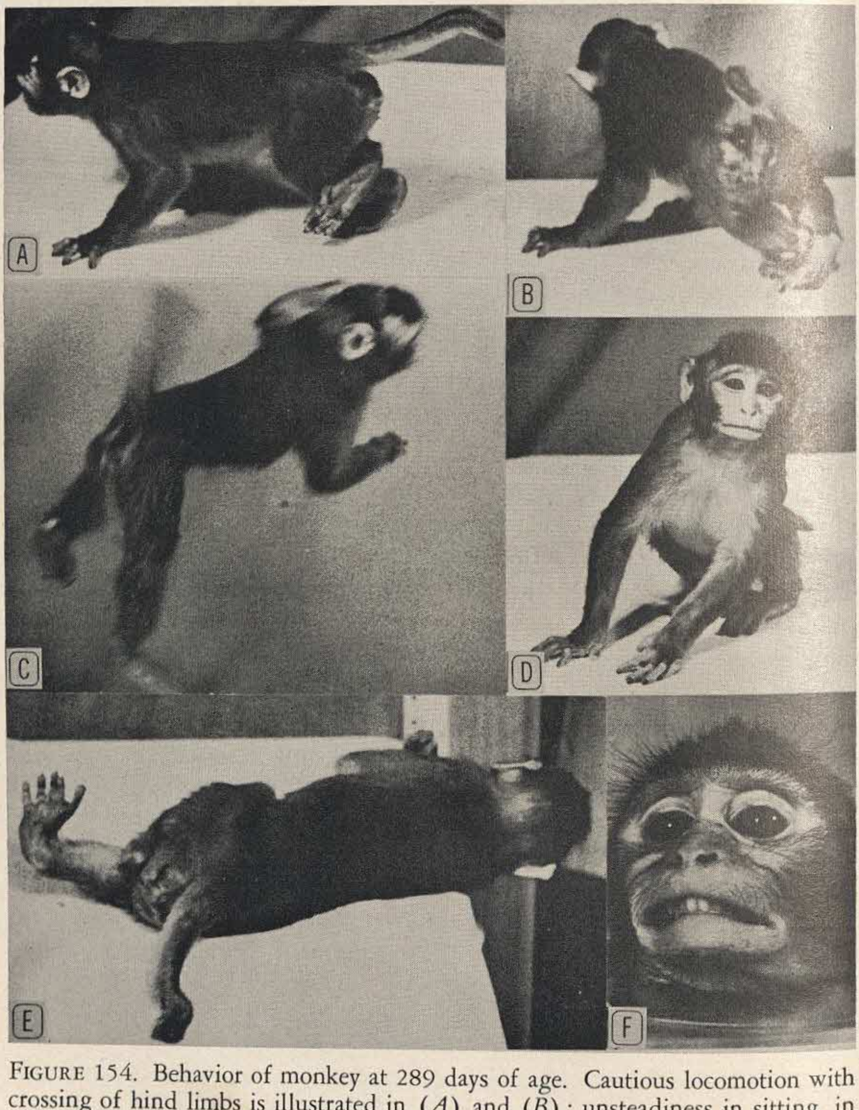

FIGURE 154. Behavior of monkey at 289 days of age. Cautious locomotion with crossing of hind limbs is illustrated in (*A*) and (*B*); unsteadiness in sitting, in (*D*). A sudden burst of motor activity results in "leaping" in (*C*). Inability to right, and uncontrolled movements are shown in (*E*); facial expressions in (*D*) and (*F*). Reprinted, by permission, from Windle, W. F., Jacobson, H. N., Robert de Ramirez de Arellano, Marisa I., and Combs, C. M.: Structural and functional sequelae of asphyxia neonatorum in monkeys (*Macaca mulatta*). *Res. Publ. A. Nerv. & Ment. Dis.* (In press).

castrated; so that, when grown up, it can scarcely have any feelings in common with the rest of its kind. From this education it has no wish to leave the flock" (3).

*Windle:* I would like to show you the technique by which we have altered behavior in monkeys.* We are studying the possible effects of asphyxiation *in amnio* of monkeys near term. The conceptus is removed by caesarean section under local anesthesia, near term. One can see respiratory movements *in amnio*. When these stop, the period of asphyxial apnea sets in. The fetus is then delivered from the amnion and we wait until the fetal heart, which has been beating around 170 per minute, decreases in rate to about 30 per minute. Then, we resuscitate by intubation of the trachea, and insufflation of the lungs with oxygen gas. In the case illustrated, the asphyxiation lasted about 12 minutes and the animal then responded to resuscitation. This was not the most severely asphyxiated nor the least severely asphyxiated of our series, but was one of the most severely brain-damaged of our animals. I will outline the life history of this one animal, until we killed him at 10 months of age. One of the most striking effects of asphyxia, from the standpoint of behavior, is the abolition of sucking. In most animals, nursing behavior was impaired, and sucking abolished, at least transiently. This animal had to be hand-fed throughout his life. The monkey was unable to right himself (Figure 154 *E*). He had a startle response, but did not respond to sound. This animal was one of only two that we have had so far with proved cerebral cortical damage. Both these animals had epileptic seizures. One of them was in *status epilepticus* and we killed him on the 3rd day. On the 7th day, the monkey was unable to right himself spontaneously. He was ataxic, disoriented, had locomotor defects (Figure 154 *A* and *B*), and was deaf. He was not blind. This animal was quiescent and we had to stimulate him to activity. There was abnormality of posture and inability to make use of his hands. When compared with a control that was a little younger, he was noticeably ataxic, hopping and stepping on his feet. The unsureness of his locomotion in contrast to that of the control was striking. Seizures then developed. There were sudden motor bursts of motor activity, mass reflexes, that threw the animal into the wall of the cage (Figure 154 *C*). The animal appeared to be unable to reach for things and when doing so, his hands went into fists. Often, he would make a supreme effort and then go over backwards and fall into one of the fits of motor activity. The facial grimaces, chewing movements, and vocalizations are quite different from normal (Figure 154 *D* and *F*).

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*Dr. Windle then showed a moving picture from which a few stills are reproduced in Figure 154.

We kill these animals by the perfusion fixation technique, and the brains are serially sectioned at 10 $\mu$, and alternate sections stained by various methods. It is a long slow process. Besides the bilateral symmetrical lesions in the frontal cortex, this animal had a central lesion in the cerebellum and extensive loss of neurons throughout the brain stem, involving most of the sensory systems (Figure 155). The auditory central mechanism was destroyed, bilaterally and symmetrically,

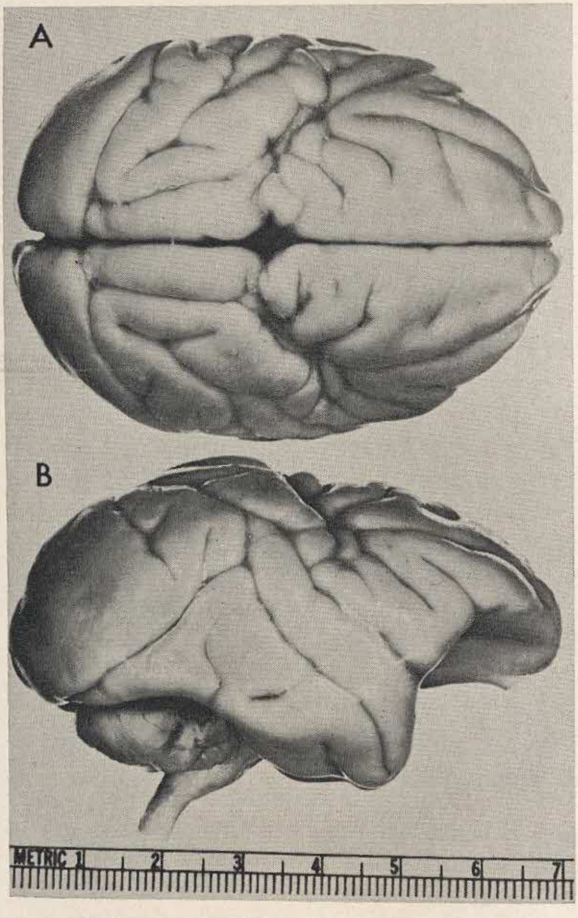

FIGURE 155. Brain of the same monkey as in Figure 154, showing atrophy in the region of the central sulci, especially the precentral gyri. Reprinted, by permission, from Windle, W. F., Jacobson, H. N., Robert de Ramirez de Arellano, Marisa I., and Combs, C. M.: Structural and functional sequelae of asphyxia neonatorum in monkeys (*Macaca mulatta*). *Res. Publ. A. Nerv. & Ment. Dis.* (In press).

and so were the medial vestibular nuclei, as well as the cuneate nuclei. The spinal cord was relatively intact. The right side is slightly more impaired than the left. From what we have been able to see anatomically, the lesions appear to be about equal. There may be some asymmetry in the lesion in the cerebellum. All animals in this series, after having been studied in various ways, physiologically and psychologically when possible, are killed.

We had an animal that was not quite as bad as this. He was born spontaneously from a mother that had hemolytic anemia. The head failed to deliver and, by the time we could complete the delivery, the monkey had been asphyxiated and required resuscitation. The histology of that monkey is identical with this one, except the cerebral cortex. He has the cerebellar and brain-stem lesions but none in the cerebral cortex. The animal did not have seizures.

*Fremont-Smith:* Was that the only difference in the behavior?

*Windle:* No. His motor behavior was not as impaired as in this one.

*Keller:* Seizures may occur later, though.

*Windle:* That is true. We have had one animal that appeared to have a seizure after several months, and then he died in coma.

Some of the animals that were less severely damaged than this one, some having been asphyxiated just short of the point of asphyxial apnea and requiring no resuscitation, have been tested psychologically by one of Dr. Harlow's students, Miss Sue V. Saxon, of our laboratory. She has found statistically significant differences in respect to their locomotion in the open-field test. The asphyxiated animals locomote more. They are less emotional than the controls.

*Fremont-Smith:* Were they diffuse lesions?

*Windle:* These are circumscribed lesions.

*Keller:* Is there any disturbance in body temperature?

*Windle:* Yes. They were poikilothermic for awhile. That is the picture.

*Fremont-Smith:* Microexamination of the normal parts of the brain did not show any diffuse, minute lesions?

*Windle:* No.

*Bodian:* Are the lesions focal rather than in the form of scattered cellular damage?

*Windle:* There was less diffuse cellular damage than sharply defined circumscribed lesions. You can see the atrophy in the region of the central sulci on Figure 155 showing the gross brain. Figures 156 and 157 show the type of lesions we are finding in these monkeys.

*Doty:* How do you explain this local damage?

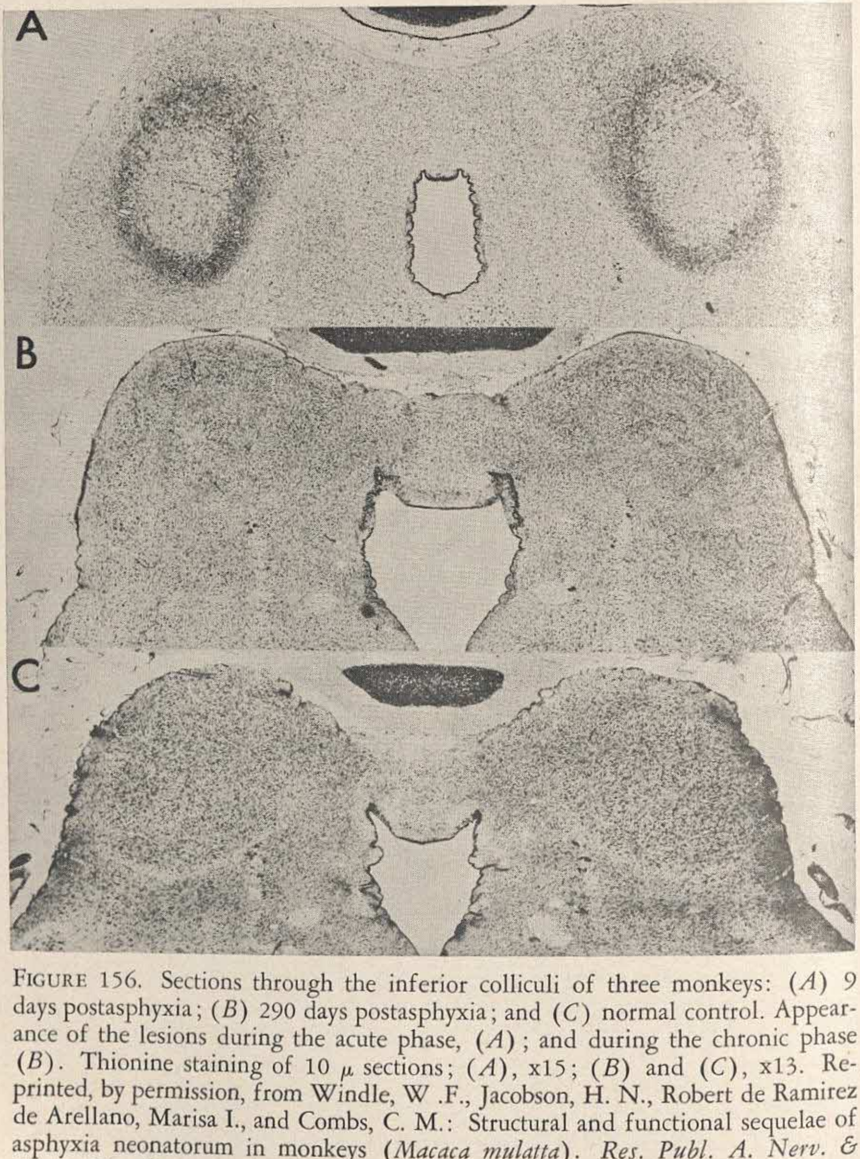

FIGURE 156. Sections through the inferior colliculi of three monkeys: (*A*) 9 days postasphyxia; (*B*) 290 days postasphyxia; and (*C*) normal control. Appearance of the lesions during the acute phase, (*A*); and during the chronic phase (*B*). Thionine staining of 10 $\mu$ sections; (*A*), x15; (*B*) and (*C*), x13. Reprinted, by permission, from Windle, W .F., Jacobson, H. N., Robert de Ramirez de Arellano, Marisa I., and Combs, C. M.: Structural and functional sequelae of asphyxia neonatorum in monkeys (*Macaca mulatta*). *Res. Publ. A. Nerv. & Ment. Dis.* (In press).

*Windle:* I don't know. I will make a guess that certain nuclei of the brain have a higher rate of oxygen consumption than others.

*Doty:* Would you say these differ, perhaps, from adult man in whom the retina is so highly sensitive, and the hippocampus seems to be highly susceptible to oxygen lack?

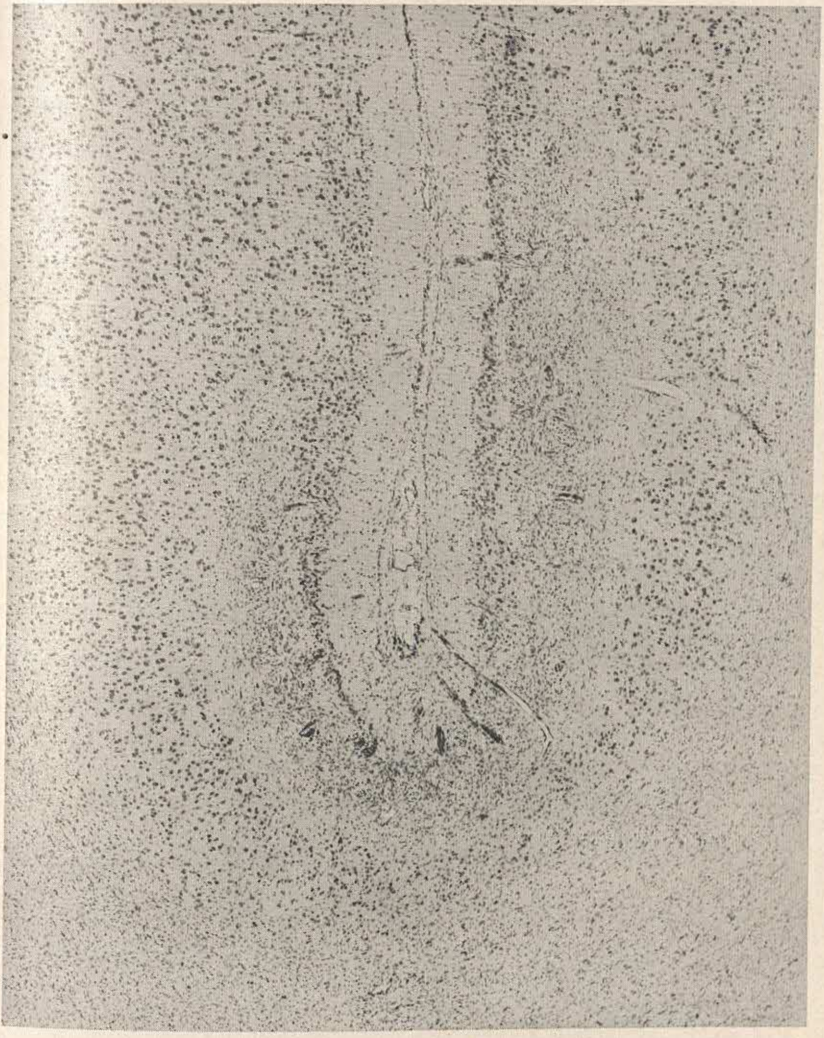

FIGURE 157. Cerebral cortex showing pseudolaminar degeneration around a sulcus (x40). Reprinted, by permission, from Windle, W. F., Jacobson, H. N., Robert de Ramirez de Arellano, Marisa I., and Combs, C. M.: Structural and functional sequelae of asphyxia neonatorum in monkeys (*Macaca mulatta*). *Res. Publ. A. Nerv. & Ment. Dis.* (In press).

*Windle:* I don't know. We have been trying to produce this same picture by asphyxiation of newborn, young, and 1- or 2-kg. monkeys, by immersion in nitrogen gas. We have not been able to reproduce this picture. We think the reason is that the fetal heart survives long enough to permit anoxia to produce neurological damage, but the heart of the newborn will not survive for a sufficient time. It fails before the brain.

*Purpura:* Dr. Windle has shown how relatively minor episodes of asphyxia at birth may produce rather profound histopathological changes in the brain. I suspect that careful examination of Golgi material might reveal marked differences in the development of superficial and deep neuropil. It is possible that even very short periods of asphyxia at birth may produce significant changes in basilar dendritic development which would not be obvious in Nissl sections. This brings up a problem relating to Dr. Harlow's attempt to vary the behavior patterns in the newborn monkey. A few years ago Eayrs (4) presented data suggesting that the development of the cortical neuropil, as observed in Golgi material, was significantly altered in cretinoid rats. Recently, Eayrs and Goodhead (5) have published additional data on this subject. Since one could readily burn out the thyroid in the newborn monkey with radioactive iodine, it would be of considerable interest to determine whether the cretinoid monkey might exhibit abnormal behavioral patterns that could be correlated with a retarded development of its cortical and subcortical neuronal interrelations.

## REFERENCES

1. Bond, D. D., Randt, C. T., Bidder, T. G., and Rowland, V.: Posterior septal, fornical, and anterior thalamic lesions in the cat. *A.M.A. Arch. Neurol. Psychiat.* **78**, *143-162 (1957).*
2. Bowlby, J.: The nature of the child's tie to his mother. *Internat. J. Psycho.-Analysis* **39** *(Part V), 374-385 (1958).*
3. Darwin, C.: *Voyage of the Beagle.* Centenary Edition. New York, Harper, 1959.
4. Eayrs, J. T.: Hypothyroidism in relation to the maturation of the cerebral cortex. In: *Biochemistry of the Developing Nervous System.* H. Waelsch, Ed. New York, Academic Press, 1955 (pp. 443-449).
5. Eayrs, J. T., and Goodhead, B.: Postnatal development of the cerebral cortex in the rat. *J. Anat.* **93**, *385-402 (1959).*
6. Luria, A. R.: Experimental analysis of the development of voluntary action in children. *Acta Psychologica* (Proc. XV Internat. Congr. Psychol.) **15**, *460-461 (1959).*
7. MacLean, P. D.: The limbic system with respect to two basic life principles. *The Central Nervous System and Behavior.* M. A. B. Brazier, Ed. Trans. Second Conf. New York, Josiah Macy, Jr. Foundation, 1959.

8. STAMM, J. S.: The function of the median cerebral cortex in maternal behavior of rats. *J. Comp. & Physiol. Psychol.* **48,** *347-356 (1955).*
9. VAN WAGENEN, G.: The monkey. In: *The Care and Breeding of Laboratory Animals.* E. J. Farris, Ed. New York, John Wiley & Sons, 1959 (pp. 1-42).

# VERBAL REGULATION OF BEHAVIOR

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I CHOSE THE TOPIC "Verbal Regulation of Behavior" for two reasons: first, because I have spent several years working on this problem, and second, and more important, because I believe that verbal regulation of behavior can play a decisive role in the evolution of brain function in man. We know that man is a social animal, and verbalization is a mode of behavior specific to man.

A great psychologist in our country, Vygotsky (34), taught that the verbal relation with the mother plays a decisive part in the further development of the child. For example, the mother says to the child, "You must take a spoon," and in this way she regulates his behavior. This verbal behavior then becomes interiorized. At the next stage, the child says to himself, "I will take a spoon." This is now autoregulation of behavior. What is at first a function shared between two persons, the mother and the child, later becomes the inner mode of the mental organization by the child himself. Therefore, development as a whole is a kind of interiorization of social conduct, creating new levels of behavior. That is why verbal regulation of behavior plays such a decisive role in development.

I hold that the most important way to study this important process is by a precise psychophysiological method, a neurodynamic approach to the analysis of how verbal regulation of behavior is developed. The success of a research depends on the selection, for analysis, of a unit of function and of the indicator by which to analyze it. If these are both well and appropriately chosen, the work will be successful. Let us begin with two experiments. A child of 1 year and 2 months knows what a fish is. I say to the child, "Please bring me the fish." The child grasps the toy fish and gives it to me. Does this mean that verbal regulation has already developed? No, for let us now come to the second experiment in which a toy cat is placed between the child and the fish. I say to the child, "Please bring me the fish." The cat is more interesting than the fish and my verbal instruction comes into conflict with the child's orienting reflex toward the cat. The child hears "fish," but although his eyes are on the fish, his hand goes out to the cat. I can tell, therefore, that at this stage verbal regulation is not yet dominant. It works only if it does not come into conflict with an immediate perception, with an immediate orienting reflex to some other more intense stimulus or one that has the quality of novelty.

Another experiment, also showing that verbal regulation of behavior is not yet operating, demonstrates a different factor. If I say to this child aged 1 year and 2 months, "Please bring me the cat" (which is on his left), he brings it to me. The same thing happens a second and a third time. But the fourth time, without changing my tone, I say, "Bring me the fish" (which is on his right), and he brings me the cat, repeating his former reactions.

Why does verbal regulation fail in this case? Because another factor, quite different from the orienting reflex, is involved. This is the factor of *inertia* of nervous activity. If two or three times my verbal instruction directed a child's movement toward the *left* side, the child needs to have a great mobility of the nervous system to be able to change this action to the *right* in accord with my verbal instruction.

From a number of experiments of this kind, it can be concluded that, in this early stage of the child's life, about 1 year and 2 months and even up to 1½ years, verbal instruction can only *initiate* behavior. It cannot yet either *stop* or *reverse* behavior. It fails when it comes into conflict with an orienting reflex or the factor of *inertia* working in a different direction.

The problem is: How can verbal instruction overcome these difficulties? How is verbal control of behavior developed to a stage at which we can, at least to a certain extent, regulate our behavior?

Passing from these demonstrations of the phenomena, let us now go to special psychophysiological experiments on its analysis. In the experiment shown in Figure 158, a child of 2 years and 4 months has a rubber balloon in his hand, and when told to press, he presses. But he does not stop his reaction, for he presses a second, a third, and a fourth time. I gave only *one* instruction, but the excitation this initiated became irradiated, and superfluous movements resulted.

My verbal instruction can start the behavior of the child at this age, but it cannot arrest his behavior. There is a similar result when I make my instruction a little more complicated. I tell the child, "Press when

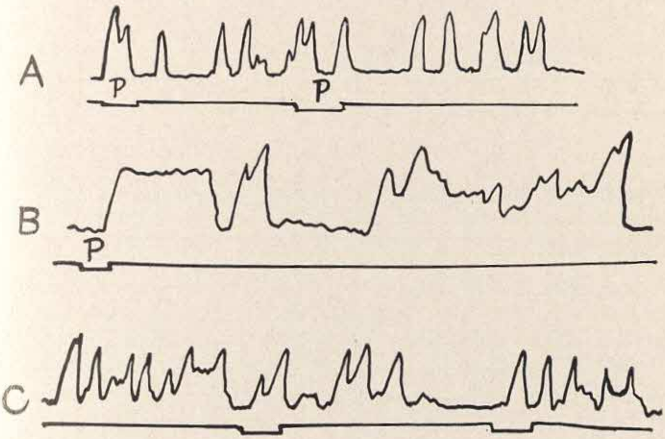

FIGURE 158. Disorganized motor reactions in very young children. The upper traces of (*A*), (*B*), and (*C*) each record the motor reaction of a child (pressing a balloon). In (*C*) only, and in Figures 159 to 163, the notches in the lower line indicate the presentation of a light stimulus. (*A*) and (*B*) record simple reactions of V. R. (2 yr. and 4 mo.) and S. M. (2 yr. and 5 mo.) to the instruction, "Press" (P). The reactions are not yet organized, for the children pressed whether or not instructed to do so. (*C*) records conditional motor reactions of V. R. (2 yr. and 4 mo.) to the instruction, "Press when you see a light." The reactions are not coordinated with the signals, for the child pressed even before any signal was presented.

you see a light." This time, the instruction is not as simple as it was in the first experiment. It is now a "conditional instruction." The child has to synthesize both components of the instruction before acting, and the light signal has to become a conditioning signal.

Figure 159 shows inhibition of motor reactions. When the child hears the instruction, "Press," he presses immediately without waiting for the light and then, when the light appears, he gives an immediate orienting reflex to the light. He doesn't press any more; he stops.

*Doty:* Would that hold even with a change of tone of voice, such as a severe command?

*Luria:* If I tell the child, "You must press once only, and please don't press after that," the additional arresting instruction from the adult doesn't help in this case, and the child presses again and again, because he reacts, not to the semantics of my instructions, but to the intensity of my voice (Figure 160). Then if I say, in different voice, "You must not press when there is no light," he does not press, but he also doesn't press even when the light appears. This is an irradiation of the inhibitory in-

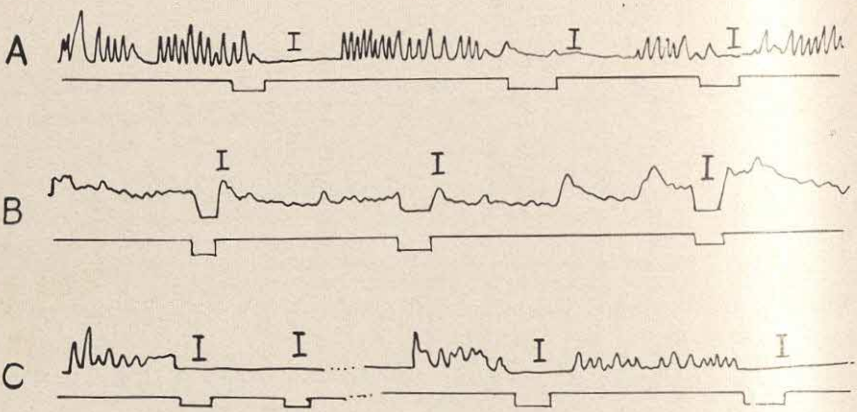

FIGURE 159. Inhibition of motor reactions as a result of an immediate orienting reflex to the signal. I = inhibition of reaction. (*A*) The child (L. L., 1 yr. and 8 mo.) responded to the verbal instruction, "Press," but the moment a light signal was presented the reaction was inhibited. (*B*) The same in another child (S. P., 2 yr. and 6 mo.). (*C*) In the imbecile child (T. G., 7 yr.), instructions resulted in an immediate motor reaction, which was inhibited by the light signal.

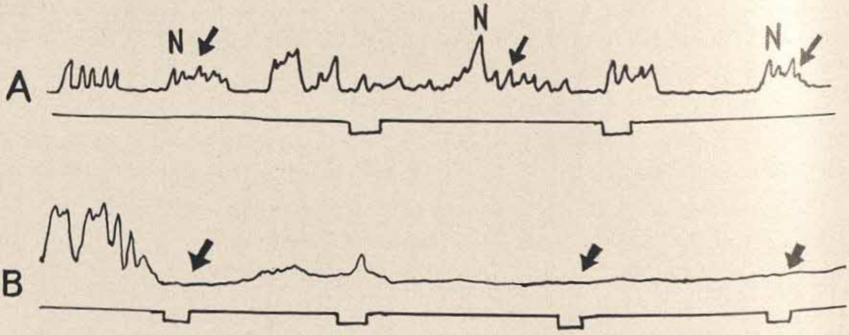

FIGURE 160. Diffuse excitatory and inhibitory reactions to verbal instructions, in very young children. N = "Do not press when there is no light." Arrows indicate errors. (*A*) Prohibitive instructions resulted in a generalized excitation. The child (K. K., 2 yr. and 7 mo.) pressed even though there were no signals. (*B*) Prohibitive instructions resulted in a generalized, irradiated inhibition and the child (S. M., 2 yr. and 1 mo.) ceased to press even though signals were given.

fluence of my instruction. I can only conclude that my verbal control of the child's behavior is not yet complete at this stage of development.

Figure 161 illustrates another method by which we try to regulate the activity of the child. If my verbal instruction does not help the child,

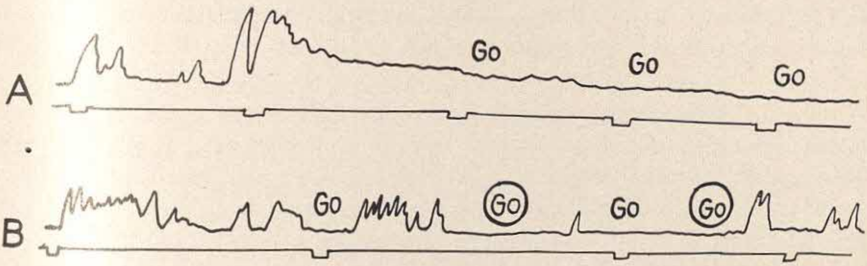

FIGURE 161. Negative interference between the child's verbal and motor reactions. (*A*) On the first two signals shown, there was a motor reaction alone, but when the child (O. O., 2 yr. and 3 mo.) verbalized on the next three signals, his motor reaction was inhibited. (*B*) On the second signal shown, the child (T. S., 2 yr. and 10 mo.) said, "Go" and made a delayed motor reaction. He later gave two verbal responses (circled) in the absence of any signal.

perhaps it may be possible for him to use *his own* verbal activity. I tell him, "You are simultaneously both a soldier and an officer. You give the order, 'Go, go,' and every time you say, 'Go,' you must also press. You have only to obey your own command." With a child of 2 or 3, this advice does not help. The neural mechanisms of the verbal reactions of the child do not yet have the necessary systemic organization or the necessary plasticity to regulate his own behavior. He says, "Go," but he is so busy saying the word that the verbalization brings a reciprocal inhibition of the motor reaction and he doesn't obey his instruction. He can do only one thing, either he can say, "Go," but then he doesn't press the bulb, or, he can press the bulb, but then he doesn't say anything (Figure 161 *A* and *B*). It is a reciprocal inhibition from one type of reaction to the other. At this stage, the verbal activity of the child himself cannot help him in the organization of his own behavior. In other words, the directive, controlling function of the child's own speech is not yet developed.

How can I arrange my experiment so that the child will be able to suppress superfluous movements? This is not easy. Since I cannot succeed by the use of the higher function of speech, I now try to train his motor reactions directly. As has been shown, in the first stage when I gave the instruction, "If you see a light, press," a lot of superfluous nonarresting movements were made. In the second stage of the experiment, I give the instruction, "When you see the light, press the balloon and put your hand on the table. Press, and put your hand on the table." Instead of having one instruction, he now has two, and the second inhibits the first, for the child puts his hand on the table and has to put the balloon aside. But that is only a starting point of the experiment. I can gradually proceed to *shorten* the child's activity. First I ask the child to press and put his hand on the table, then to press and put his hand near the balloon, and then to press only (Figure 162). I thus gradually reorganize his behavior in several steps: first, replacing the reaction at A with direction B withdrawing the hand, then putting the hand on the balloon and developing an inhibition by reduction of this second external action. That is the mechanism of training an inhibitory process. After such training, I can obtain good control in a child of 2 years and 4 months, without using his own verbalization.

Next, I come to the question: Is it possible to arrest the superfluous movements of the child by a different technique? Let us analyze the factors which made the immediate voluntary inhibition of the child's superfluous movements impossible. Why is the child unable to organize his own movements and arrest his own activity? I believe it is not only because his speech has not yet acquired a regulatory role, but also

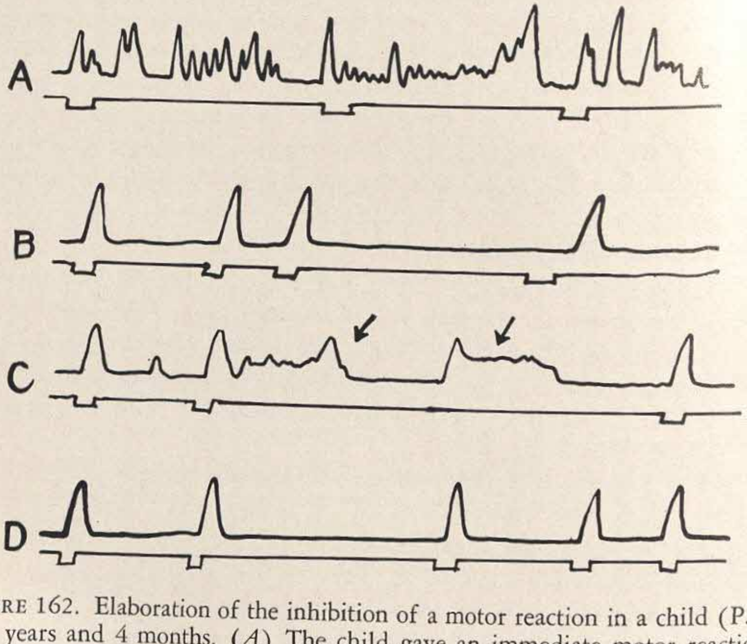

FIGURE 162. Elaboration of the inhibition of a motor reaction in a child (P. A.) of 2 years and 4 months. (*A*) The child gave an immediate motor reaction to the signal. He was allowed to hold the balloon in his hand all the time. (*B*) The child had to put the balloon on the table after every signal and remove his hand. (*C*) With the balloon in his hand, the child began to make errors. (Arrows indicate errors.) (*D*) Continuation of same experiment. Gradual organization of the movements is shown, and coordination of the movements with the signals.

because the afferent feedback from his own movement is not yet ready at this age. I don't think the child, at this stage, gets good proprioceptive signals from his own movements, signals which should arrest the action at the right time. What will happen if I replace the missing proprioceptive feedback signals for arresting the movement by an exteroceptive signal, if I endow this exteroceptive signal with an arresting function?

The experiment is as follows: I instruct the child, "Press the balloon, and when you press it, you will hear a sound. This sound will be a signal for you to stop pressing." This is a concrete exteroceptive signal which arrests the movement, and the missing regulatory role of verbal instruction and of kinesthetic signals is replaced by a strong and concrete exteroceptive signal with a feedback action. S. V. Yakovleva, in my laboratory, has proved that, in many children, such direction by concrete exteroceptive feedback can result in an organization of motor reaction in cases where the direct method fails. Figure 163 gives an illustration of that experiment.

If it is possible to do this in cases when the child is only 2½ years of age, perhaps things will be different at the next stage of development.

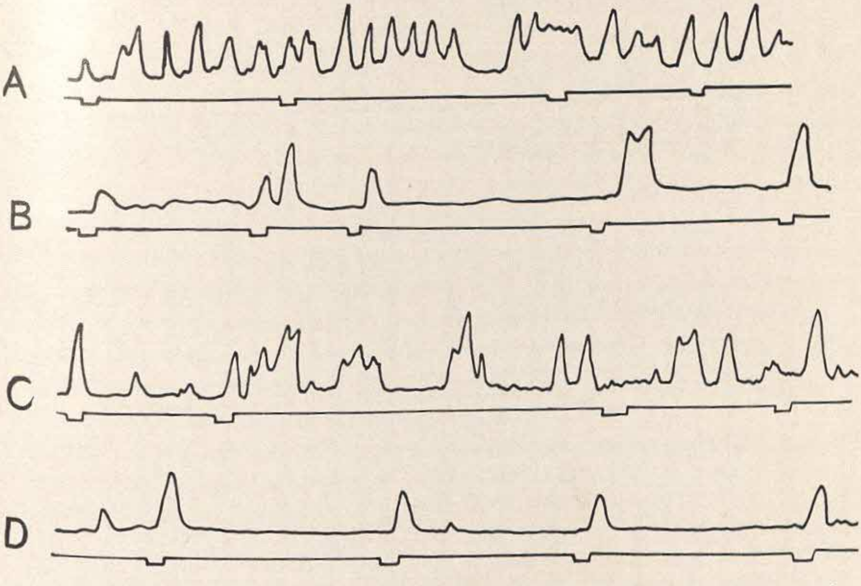

FIGURE 163. Reinforcement by exteroceptive feedback from the ringing of a bell. (*A*) Responses to signal without feedback from bell. (S. M., 2 yr.). (*B*) The same child pressed when he saw the signal and heard the bell. (*C*) and (*D*) Same experiment in another child. (Z. L., 2 yr. and 4 mo.)

First, let us show how a system of voluntary reaction to a verbal instruction—a positive to one signal and a negative to a second signal—can be obtained in children of different levels of the pre-school age. This is shown in the records of Figure 164. In these experiments, we give to these children of 3, 4½, and 5½ years of age a more complicated task: The child must discriminate between two signals, a red (R+) and a green (G−) one, each with its special signaling function, positive to

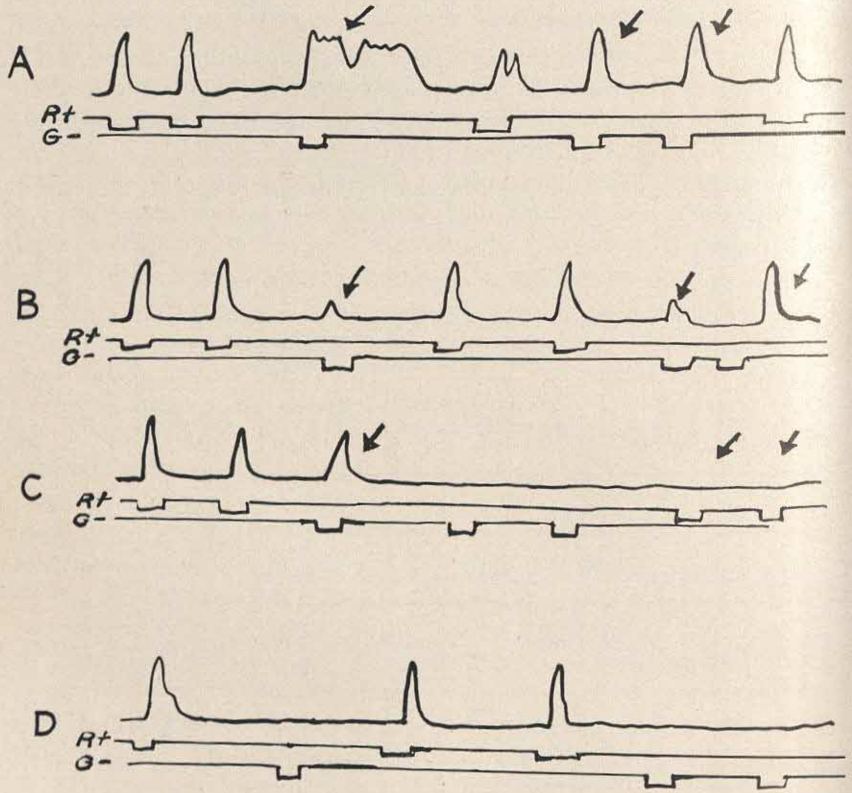

FIGURE 164. Motor reactions to differential signals in children of pre-school age. The upper traces of (*A*), (*B*), (*C*), and (*D*) record the motor reaction of each child (pressing a balloon); the center line is the signal for a red light (R+); and the lowest line is the signal for a green light (G—). Instructions to the children were to press only on the red light signal. Arrows indicate errors. (*A*) and (*B*) The 3-year-old child (S. B.) pressed indiscriminately to both colored lights. (*C*) The child of 4 years and 6 months (R. K.), after one error to the red light (R+), correctly inhibited his reaction to the green light, but this inhibition irradiated and suppressed response to the red. (*D*) The child of 5 years and 6 months (V. T.) differentiated the signals correctly.

the red and negative to the green. Instructions are, "If you see a red light, press. If you see a green light, do not press." The results obtained in all three cases are different. The child of 3 years preserves the instruction and can repeat it quite well. He says: "If I see the green, I shall not press." But all the same, he presses to all lights (Figure 164 *A*). His knowledge does not help him to follow the verbal instruction and to regulate his behavior. A partial arrest of behavior can be seen in this experiment, but the effect of inhibition is very short. Then, even this partial arrest disappears and the child presses to the negative signal as well as to the positive one.

Also in Figure 164, typical results are shown for a child of 4½ years (Figure 164 *C*). These are different from these of the 3-year-old. The negative part of the verbal instruction is very short too; but if I reinforce the negative meaning of one of the signals by repeating, "When you see a green light, don't press at all," the child doesn't give any reactions to the negative signal, but now he does not react to the positive stimulus either. This is an irradiation of the inhibitory role of the speech instruction; so the child is still not yet ready for full organization of his behavior by control of the preliminary verbal instruction.

At 5½ years of age, this form of organization of motor behavior is completed (Figure 164 *D*). The plasticity of the nervous system is now well developed, and the child's motor reactions can obey the command of the second signaling system; a good system of positive reaction to the red and a negative reaction to the green signals is ready. All these data show that only in the fifth or even sixth year of the life can a verbal instruction provide a stable system of positive and negative motor reaction for a long period of experiment.

Is it possible to obtain the same results in a young child of 3 years of age? What methods of organization can provide a stable control of motor reactions at the stage when a preliminary verbal instruction is not yet able to produce a controlling effect? The experiments show that such a controlling function can be taken over by a system of permanent sanctioning reinforcements from the adult.

Figure 165 illustrates such a case. A child of 3 years of age is unable to give a stable system of positive and negative reactions to red (R+) and green (G−) signals if every reaction is not reinforced. But if we reinforce every reaction of the child by saying, "Yes, right," after correct reactions, and, "No, no!" after he makes errors, a system of correct reactions is formed in a short time. At this stage, in a 3-year-old child, a controlling function of the preliminary instruction is not yet ready; reinforcement can come only from outside, from the adult's

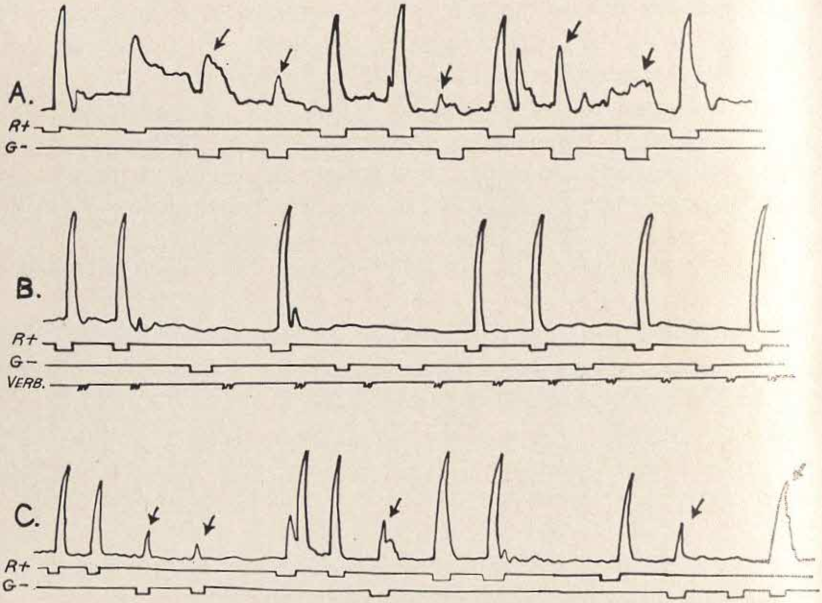

FIGURE 165. Elaboration of differentiating reactions in a child (K. B., 3 yr. and 6 mo.). (From the work of N. P. Paramonova). Arrows indicate errors. (*A*) Differential motor reactions in response to verbal instructions: "Press when you see the red" (R+). "Do not press on green signal" (G—). Partial inhibition resulted. (*B*) The upper three lines signify the same as in Figure 164, (motor reaction, red light, and green light) and the fourth line indicates verbal reinforcement (VERB.) by the experimenter, who said, "Right," when the child responded correctly. (*C*) The same experiment but without verbal reinforcement by the experimenter. The child made errors.

evaluation of every separate reaction. That is the stage when the voluntary action can be provided only from an interaction of two persons, the adult and the child (34). That is why merely leaving out these permanent reinforcements causes the stable system of positive and negative reaction to disappear. As indicated by arrows, in Figure 165 *D*, many disinhibited motor reactions can be observed after the permanent external reinforcement is left out.

*Pribram:* May I point out something here that is very important from the theoretical standpoint? We are using the word, "reinforcement," synonymously with "instruction." This is hardly new, except to those who have been thinking of reinforcement exclusively in terms of drive and need reduction.

*Luria:* No! Reinforcement here has a different meaning. It is my indication to the child as to whether the result is correct or incorrect. It is an evaluation of a coincidence of the reaction with the expected results that have been created by the verbal instruction.

*Reynolds:* Is the child's reaction to its mistake important, for example, whether it is amused or angered?

*Luria:* It is very important, but one should remember that this is a child of only 3 years.

Figure 166 brings us to the decisive point of what I want to report. At the 3-year-old stage, verbal activity is highly developed, but the neurodynamics of the verbal reactions of a 3-year-old child are quite

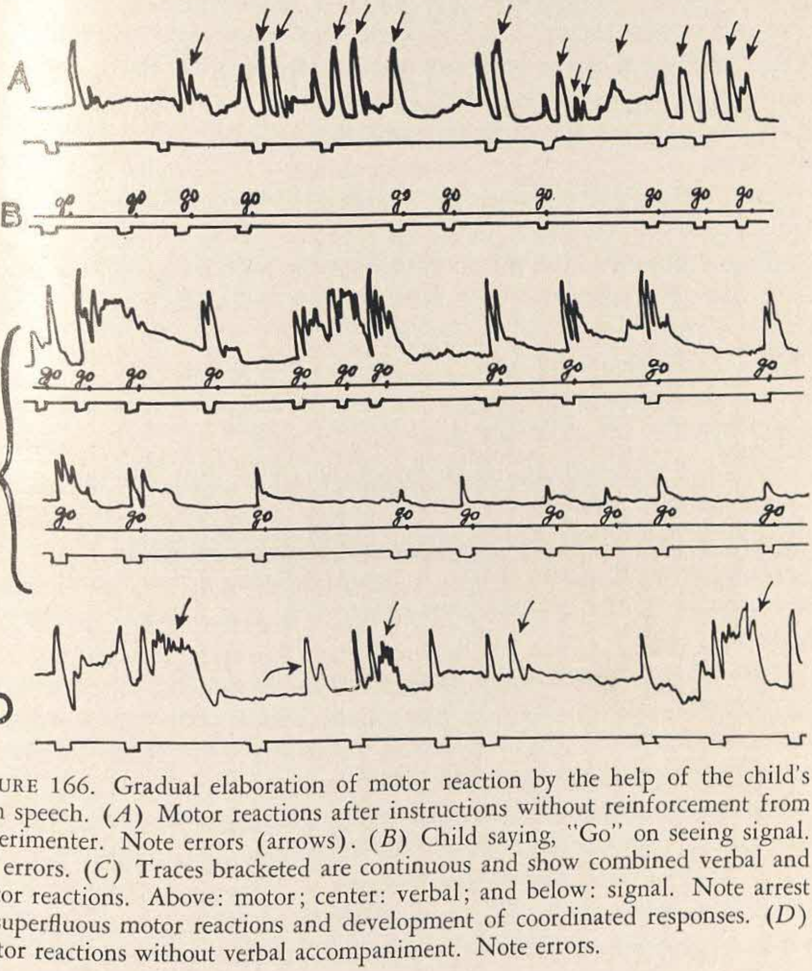

FIGURE 166. Gradual elaboration of motor reaction by the help of the child's own speech. (*A*) Motor reactions after instructions without reinforcement from experimenter. Note errors (arrows). (*B*) Child saying, "Go" on seeing signal. No errors. (*C*) Traces bracketed are continuous and show combined verbal and motor reactions. Above: motor; center: verbal; and below: signal. Note arrest of superfluous motor reactions and development of coordinated responses. (*D*) Motor reactions without verbal accompaniment. Note errors.

different from those of the verbal reactions of a child of 2½ years. The process has become more concentrated, more mobile, more plastic, and has a new potentiality.

This is the stage at which I really can apply the verbal reactions of the child himself to the organization of his own behavior. This is illustrated in this chart. The first experiment is the same as the previous experiments, "Press when you see a light." There are correct responses and some additional superfluous movements. In the second experiment, the motor reactions of the child are replaced by his verbal reactions. I say, "Don't press the balloon. Simply answer, 'Yes,' when you see the light." The child, when he sees the light, has to give only the verbal answer, "Yes." The result is quite different. He doesn't say many, many times, "Yes, yes, yes, yes." He answers, "yes" every time he has a signal. The mobility of the verbal reaction is higher than the mobility or plasticity of the motor reaction.

*Fremont-Smith:* What do you mean by "mobility" or "plasticity" in this case?

*Luria:* The Pavlovian term is "Podviznost." Its translation is mobility, plasticity, flexibility. The motor response of the child at this stage irradiates too much, but the neural processes underlying verbal reaction have more plasticity than the nervous processes underlying the motor reaction of the hand.

*Fremont-Smith:* But there is a motor component in the verbal response, so you are saying that the motor response of speech has more plasticity than the motor response of the hand.

*Luria:* Yes, but these motor responses are at different levels. The motor response used in verbalizing has, at this stage, a better neurodynamic organization than the motor response of the hand.

*Livingston:* Professor Luria, is this a process of individuation as it proceeds from the cephalic end downward, and would foot control come still later?

*Luria:* Yes, those are the levels of organization, but the regulatory property comes from above. Control by his own speech is impossible for the child of 2 years. But an older child can obey when told, "When you see a light signal, say, 'yes' and press."

*Keller:* But there is another factor, Professor Luria. When you say, "Go, press," you are, in a sense, talking in code. It is not direct.

*Luria:* Yes, and there is another factor. When you have a balloon in your hand you get a reaction from the skin and the muscles. It is a kind of grasp reflex. There is no such factor in a verbal reaction.

*Keller:* That's right; so it might not be a level of integration. It is a code.

*Luria:* Yes, therefore the verbal reactions are at a better stage of development than the hand reactions. But this still does not mean that a child of 2½ years can use his verbal reaction, for this is still too unorganized.

*Purpura:* The problem concerning the relative development of different cortical areas subserving motor activities in the newborn animal was investigated by Langworthy (19,20). The latter found that in the cat the area presiding over foreleg movements was more fully developed at birth than the hindlimb and face areas. Langworthy's conclusions were based on the effects observed after electrical stimulation of pericruciate cortex. He also noted differences in the histological development of different regions in the motor cortex which, presumably, correlated with the physiological observation. Forelimb movements were apparently obtained before movements of other parts of the body.

*Bridger:* Perhaps I can explain some Pavlovian terms. In respect to strength, Pavlov meant the size of the conditioned response as related to the strength of the conditioning stimulus. Balance refers to the balance between inhibition and excitation, which is measured by how many trials are required to obtain conditioning as compared with how many trials are required to extinguish or get differentiation. By mobility, Pavlov meant the ability to switch from positive to negative stimuli and back again.

*Brazier:* Professor Luria, while we are discussing the use of terms, would you explain for me how you are using the word, "irradiated"?

*Luria:* I mean by this that it is impossible to stop the reaction that was provoked by my stimulus. It continues.

*Brazier:* You are not thinking in neurological or neurophysiological terms?

*Luria:* In this experiment, I do not have the grounds for doing so.

*Fremont-Smith:* And is "irradiation" analogous to "perseveration?"

*Luria:* Yes, "perseveration" is a very common term among clinicians, and a very good one. In the experiments I am describing, I start from two facts: there is poor voluntary inhibition in the hand and good verbal reaction even without additional external reinforcement. We combine both and tell the child to dictate to himself and to obey himself. This is not easy for a child of 3 years and 9 months, but he can be trained to do it.

The result is illustrated in Figure 166 *C*. The child says, "yes," and presses many times. This is a very complicated process, but after a series of training sessions, quite good reactions are developed. He says, "yes" and there are no superfluous movements; so he is now reaching a very important stage. After some combinations of verbal and hand reactions, the verbal reaction of the child begins to play a controlling role over the hand movement. We have created an artificial functional system with the leading control being the verbal command from the child himself.

*Fremont-Smith:* Isn't the verbal command in each case producing an orienting reflex which inhibits the other?

*Luria:* Perhaps. The next stage, which I have not yet done but in which I think we shall collaborate with Professor Sokolov, is to combine this method of registering motor reaction with his method of analysis of the orienting reflex. This would be a step further in the investigation of the mechanism behind the result we have produced.

If we leave out speech reaction and once again tell the child not to speak, he returns to his previous behavior. He makes many superfluous movements, as can be seen in Figure 166. There are sometimes some appropriate reactions, but only sometimes. This is the stage when verbal reaction is necessary for the child in organizing his own hand movements.

*Kelly:* What impresses me in Figure 166 is that the child's verbal reaction seems to come after his motor reaction rather than before. Instead of giving himself the verbal command and then pressing, he is pressing and then giving himself the verbal command.

*Luria:* Yes, at this stage, the coordination of verbal and motor reactions is not yet well developed. That is why the child sometimes presses and then speaks, and sometimes the reverse. Imbecile children have the same difficulty.

*Bodian:* May I just suggest the possibility that, instead of the hand activity, one might try opening of the mouth, without verbalization?

*Luria:* I have not tested for that. It is a good idea.

*Reynolds:* I have something relevant to that. At one time, I was trying to count heartbeats of microcrustacea. These are very difficult to count because they are so fast, and as I had no method of counting this electrically, I found it impossible. I was not trying to verbalize; in other words, I wasn't trying to voice "1, 2, 3," but I was trying to say, "1, 2, 3," mentally. I discovered that I could synchronize the clicking of my teeth, that is, a jaw movement. I could move my jaws rapidly enough to keep up with the heart beat of this crustacean and, by doing that, I was able to keep count. In other words, with this jaw movement, I was able to keep track of the numbers, which I could not do without the jaw movement.

*Luria:* Yes, because at your developmental level, the muscles of your mouth, which are part of the speech system, have more "mobility" (in the sense in which we have been using this term) than have the muscles of other systems. The word "mentality" lies in another realm of discourse. You have changed the semantics. Let us continue with the experimental findings.

Figure 167 shows a typical effect in a child of 3½ years of age, not the process of gradual learning of verbal organization, but the result. In the absence of any verbal instruction, there are superfluous movements. The organization of the movement fails because there are no external regulating verbal components. With the verbal instruction, "Go, Go, Go," the performance is all right.

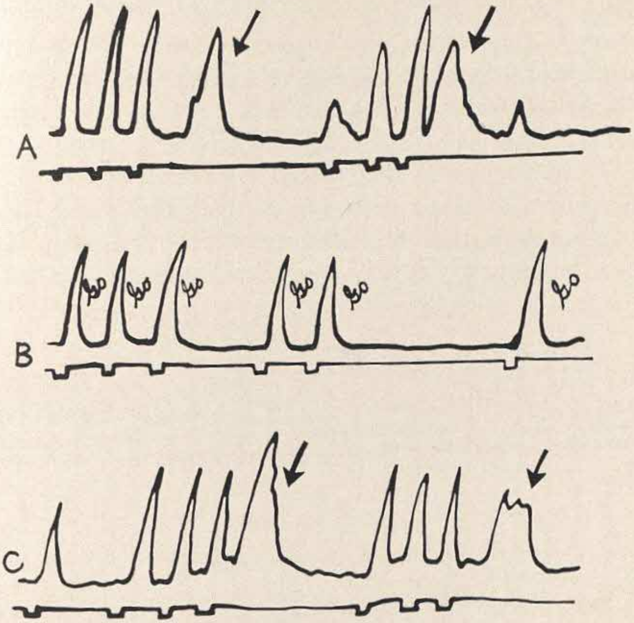

FIGURE 167. The regulating influence of the child's own speech on his motor reactions (L. P., 3 yr. and 6 mo.). The notched lines indicate the presentation of a light signal. Arrows indicate errors. (*A*) Without verbal accompaniment, the child responded to each signal but failed to inhibit response on omission of signal (disinhibition). (*B*) With each motor reaction, the child said, "Go," and responded correctly throughout. (*C*) Once again the verbal reaction was omitted and the disinhibited motor reaction returned.

Figure 168 is the record of a child of 3 years. If I make the signal long, he responds with a long movement, very long signals and very long movements. It is an echopraxic reaction. The movement reflects the length of the signal, of the excitation. It is a mirror phenomenon which we often see in clinics.

The child is, to a degree, a slave of the signal, of the physical properties of the stimulus. A long signal evokes a long movement; a short signal, a short movement. But if I introduce the speech of the child, something quite different happens. To a short stimulus, he says, "Go," and to a long stimulus, he says, "Go," but the movement is not a mirror movement. It no longer reflects the length of the signal. He coordinates his hand movement, not with the stimulus, but with his own verbal reaction. That is very significant, because it shows the mediating role of the verbal reaction in organization of the movement.

It is evident that in this child the verbal system is not yet ready for this. He says, "Press," and he presses. He says "No," but he presses. Why? Because—and this is a very important point—the speech reaction has two properties, a semantic one and an excitatory one activating the motor response. In positive reactions, both activities are excitatory and therefore of the same class. The reaction (of saying "press") is positive semantically and positive in the excitation of a movement. There is a motor excitation both of the hand and of the speech apparatus. But in the negative reaction, both reactions are not of the same class. The child gives a semantically negative reaction, but an excitatory positive

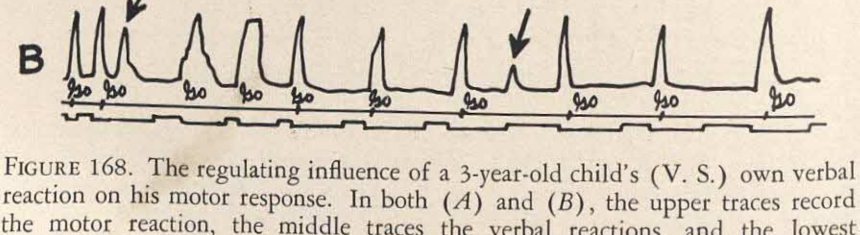

FIGURE 168. The regulating influence of a 3-year-old child's (V. S.) own verbal reaction on his motor response. In both (*A*) and (*B*), the upper traces record the motor reaction, the middle traces the verbal reactions, and the lowest (notched) lines indicate the presentation of light signals. Arrows indicate errors. (*A*) The motor reaction to the signal without speech. (*B*) The same, with the child saying, "Go," every time he responded by pressing a balloon.

motor reaction. At this stage of development of language, the child obeys, not the semantic content of the verbal reaction, but its excitatory property. The child says, "No," but he presses.

Figure 169 is the evidence in this experiment. The experiment is designed so that the child has to answer with a "yes" and press to the positive signal; on the negative signal, he must withhold both motor and verbal reaction. Both the motor and the verbal responses now have to act in the same direction and he succeeds on the red light (R+). He says "Yes" and he presses. On the green light (G−), he says nothing and does nothing. There are no failures. At this stage, the regulating influence of speech can be utilized only if there is no conflict between the semantic direction of the word and the innervatory excitation of the movement.

If there is a conflict, the child, on getting the negative signal, reacts, not to the semantic, but to the excitatory aspect of the signal.

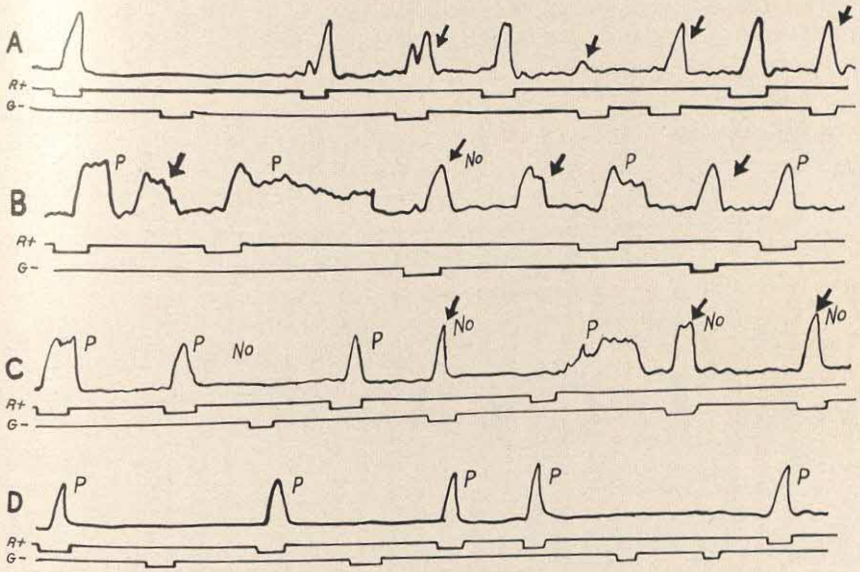

FIGURE 169. Role of the child's own verbal reaction in elaboration of positive and negative responses. Instructions were to press on red (R+) and to refrain on green (G—). Arrows indicate errors. (*A*) Without the child's speech. (*B*) Same, but child now said, "Press" (P) with response and "No" when he refrained. Note at arrows extra motor reactions in absence of signal. (*C*) The same child after training. There were two errors (arrows) where there was disinhibition in spite of child's saying, "No." (*D*) Instructions were, "Press and say 'Go' when you see red; be silent and do not press on green." No errors.

*Brazier:* Professor Luria, how do you capture the interest and attention of so young a child to do this?

*Luria:* That is one of our most difficult tasks, and we have to make many tests before we can start the real experiment. At the first testing, the child does not have sufficient incentive so we can't really start.

*Fremont-Smith:* Can you get such a child to cooperate consistently with you, or is it only every now and then that you get enough attention from him to get a reliable experiment?

*Luria:* The experiment has to be short, and there has to be some incentive. If we design the experiment as play for the child, he does better than when it appears to be work.

Figure 170 illustrates a different experiment. I instruct the child to

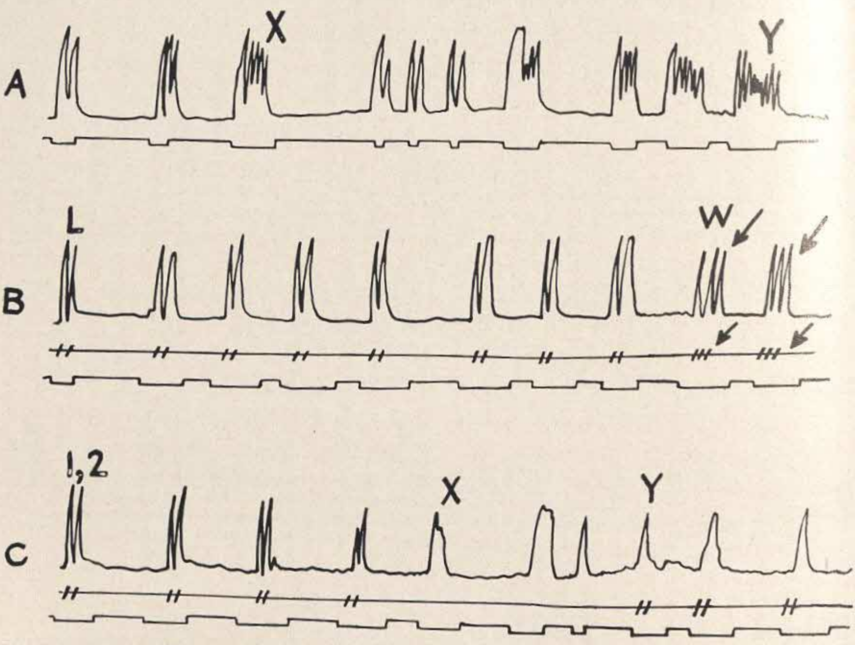

FIGURE 170. The regulating role of the child's speech on complex motor reactions. The hatched lines indicate the child's verbal responses and the notched lines the presentation of a light signal. (*A*) Child was instructed to press twice on seeing a light. Asked how many times he had pressed: at "X" he answered, "Twice," and at "Y" he answered, "Three times." (*B*) Same, but child told to speak when pressing. Left, instructed to speak loudly (L). Right, instructed to whisper (W). Note correct responses when he spoke loudly but perseveration when he whispered (arrows). (*C*) Child instructed to press twice on each signal and to say ,"1, 2." At "X," asked how many times he had pressed, he answered, "Twice." At "Y" after being told to press twice, he said, "Twice."

press twice to every signal. The child gives two, three, four, even five or six reactions, but he cannot reach a real control of pressing only twice to each signal.

However, when I tell the child to add his verbal comment to this instruction, he can perform correctly. I ask him to say, "Toot, toot." That has no meaning. It is only a verbalization but he obeys, and there are almost no failures. But if I say, "Give your answers in a whisper," the regulating role of speech is diminished. Failures occur. Instead of saying, "Toot," only twice, he begins to say, "Toot, toot, toot; toot, toot." This is a perseveration in speech and it brings on a perseveration of the motor reaction as well.

In the next part of the experiment, I say to the child, "On every signal, don't say, 'Toot, toot,' but say 'I press twice.' " He says, "I press twice," "I press twice," but he presses only once. Why? Because the dominating influence is not the semantic meaning but the motor component of the speech reaction.

*Lilly:* I was trying to separate out the motor component of the speech from the acoustic feedback to himself, and wondering which one is the limiting factor.

*Luria:* In this experiment, I am separating the semantic component from the motor component of speech. I have not investigated the acoustic feedback.

*Bodian:* Because of the high interest of the complicated verbal response, has he lost interest in the motor response?

*Luria:* I am not at all enthusiastic about trying to guess what the child is interested in. I don't know. But I know the objective result of his behavior. Every time I bring the motor component of the verbal reaction into conflict with a movement of the hand, the motor reaction fails; so I have tried in other experiments to make the child press weakly, and to give himself a command in a loud voice. In all cases, the decisive role was played, not by the semantic side of the speech, but by the muscular characteristics. That is why I think this is a real stage in the development of speech, one in which the motor component of speech can organize the child's behavior but the semantic side cannot yet do this.

*Fremont-Smith:* Suppose you reversed the order; suppose you gave the child a command to say, "Toot, toot," and he was then to reinforce this by pressing the bulb. Would you get the same results? It seems to me that this would be interesting because it would make a differentiation between the higher level of the speech activity and the motor level. It may be that there is a time sequence which is important here, rather than the higher activity, although I suspect the higher activity is the dominant one.

*Luria:* I don't know. It is an open question.

*Leese:* Professor Luria, in experiments of this type, have you tried to modify the motivation in these children by a system of reward and punishment?

*Luria:* I have tried but failed, because, when I say, "You will get a candy for this," the child becomes so interested in the candy that he fails in his work. It is not a simple matter to increase the motivation of the young child in this experiment.

*Kelly:* In this type of model that you have given us here, is the speech serving as the orienting reflex?

*Luria:* Yes. I think that is the mechanism. The use of speech enhances the orienting reflex.

*Leese:* But an orienting reflex, if I understand it correctly, and I suspect I don't, does not ever serve an inhibitory function, is that right? Does it ever serve as an inhibitor?

*Luria:* The preliminary orienting reflex is a factor essential to every conditional reflex. When a conditional reflex is inhibitory in function, the orienting reflex will be conditioned to arrest movement. You can't arrest movement without attention, without orienting.

*Leese:* So it can serve, then, in that capacity.

*Luria:* Yes, I think so.

*Sokolov:* I believe it is well known that external stimulation produces the so-called external inhibition of a conditional reflex. This is the influence of the orienting reflex, produced by external stimulation, upon the conditional reflex. Therefore, the orienting reflex, although being at the same time a kind of excitatory response, can influence the conditional reflex in an inhibitory manner.

*Luria:* I would like to summarize the material I have presented. After a series of experiments, of which I have shown only a few, we have reached a theory about the development of the regulatory function of speech in the child. This sequence of steps of verbal development in the child proves to be much more complicated than we had originally thought. The first stage is when the child's verbal activity cannot yet play a decisive role in the organization of his own behavior. The second step is when the child's verbal activity begins to play a regulating influence on his behavior, but is not yet complete. At this second stage, the semantic side of speech does not yet have a decisive influence. For the semantic side of speech, if it comes into conflict with the external motor function of speech, fails.

Only at the third stage does the semantic side of speech begin to play a really decisive role. For at this third stage, it is not obligatory for the child to apply externally vocalized speech, because at the moment when semantic control is developed, the child can use his internal subvocal speech. As a result of this interiorized process, the child can obey instructions without speaking loudly and without using the reinforcement of his own externally heard speech.

I should point out that speech has different roles—a nominative role, a generalizing or semantic role, a communicatory role, and a regulating role. The regulating or controlling influence of speech had not been as well investigated as the others, and that is why we focused attention on it, for it is very important in the problem of the mutual relationship of the two signaling systems. I have presented examples from a series of experiments on the organizing regulatory role of the second signal system in motor reactions.

*Doty:* I have a question concerning the very earliest development of, not speech *per se*, but of linguistic recognition, the recognition of spoken words by the child. It seems to me, from what we might call purely naturalistic observations in the home, that a child picks this up almost in the way Dr. Hess's birds are imprinted on an object, simply by pure exposure, without motivation on the part of the parents or without the parents even realizing that the process is occurring. Thus, by this purely associational process, the child can then recognize and select objects named to him. Do you agree that this occurs?

*Luria:* Yes, in the psychological literature there are very good studies from both Europe and America. Werner (36) in Worcester has made some excellent investigations of the different stages of speech development. But I should perhaps mention an experiment by Fradkina (10) and Lublinskaya (24) in Leningrad. When a child is presented with a doll, a puppet, and asked, "Where is the head?" he points to the head. When, after tearing off the head of the puppet, you ask, "Where is the head?" he points to where the head used to be. So it is not the object that the child points to, it is the reproduction of a certain movement.

In another experiment, a picture of the child's father is used. You say, "Where is your father?" The child points to the picture. You remove the picture and says, "Where is your father?" And the child points to the same place where the picture used to be.

A very intensive series of experiments in this direction has been made by Koltzova (18) in the Physiological Institute of the Academy of Sciences in Leningrad. She investigated stages in the grasping of the meaning of speech. At the very first stage, in the infant, the child grasps or understands speech only if it is speech from his mother, spoken in a certain voice, and if the child is lying in a certain position. Changing the position of the infant is enough to upset the understanding of the words. In the second stage, although the position of the child may be changed, the meaning of the words remains, though if the voice is changed, the meaning is lost. In the third stage, you can gesture, change your gesture, or omit the gesture without the child's losing the semantic meaning but if you change your voice, the meaning disappears. These stages have been very well and precisely studied in many, many experiments.

*Roberts:* When the signals become interiorized, could you still get potentials from the vocal cords?

*Luria:* Yes. On that point, I have to refer to another series of experiments. In one of our recent conferences, we devoted a whole session to the subject of electromyographic recording of subvocal reactions. It has been found that, in several stages of subvocal actions, action currents of the muscles can be recorded, though not at all stages. Muscle action currents can be recorded only in the first stage of interiorization. In the last stages of interiorization, we have not found any action currents by our methods of recording.

*Fremont-Smith:* When you say the "first stage," do you mean ontogenetically or in a special experiment?

*Luria:* I mean the first stages of training. These experiments were done by Alexander N. Sokolov (31).

*Harlow:* Would the fundamental design of these experiments be altered if the child were to press a lever instead of a bulb?

*Luria:* If a lever were used, some of the components of the grasp reflex would be eliminated, but the effects would be the same.

*Sokolov:* I should mention that the appearance of the muscle tension during internalization of the voice depends on the difficulty of the task presented in the experiment; for example, a decision about some difficult differentiation will again evoke these muscle tensions as evidenced by action currents.

Of interest is the fact that this functional system, in normal development, is connected with a change of the mechanism of the tongue and the system of voice, but in the case of deaf mute children, it is connected with the hand. During the thinking of the deaf mute child, increased muscle tension is registered in the hand, because gesture is connected with this mechanism.

*Luria:* I can add only one experiment in this connection. One of my aspirants (post-graduate students) wrote her thesis on the analysis of external speech mechanisms in writing. For example, when you write a very complicated word such as "oligodendroglia," you have to verbalize it in order to spell it correctly. We noticed that this was a very interesting question for pedagogy. If you go into the first grade in a Russian school when a lesson in the Russian or the German language is being taught, you will observe that the children are mumbling. Why do they not mumble when they are being taught English? Because the English language has a quite different structure. The spelling in English does not coincide with phonetics. It is not a phonetic language and to verbalize does not help them to spell correctly. The problem in pedagogy is whether this verbalization in the first grade is good or not.

To test this, I asked my aspirant to make the following experiments: Experiment 1, the child had to verbalize while writing. Experiment 2, the child had to write while holding his mouth wide open. The result was that there were six times as many mistakes when the child could not verbalize. Without verbalization, there is no analysis of the phonetic structure of words, so, in the first grade, it is necessary to verbalize. In the third grade, it is not obligatory. In the fifth grade, it is bad. However, as I said, this does not hold for the English language or for French or for Chinese, as they are not languages with phonetic spelling.

*Magoun:* I have been impressed by how little investigative work has been undertaken in the field of language and speech, considering that it is the most uniquely important performance of man, as distinguished from the lower animals, and I wanted to ask whether you or others in the USSR have employed visual rather than auditory signals in this kind of experimentation, using the 6- to 8-year-old child. In addition to your use of the spoken word and the auditory analyzer, have you made analogous experiments, using the visual analyzer at a somewhat more mature stage, when the child is able to read? Analogously, have you or others made an analysis on the motor side, employing written rather than vocal symbols? Are these kinds of experiments being done?

*Luria:* Yes. I presented the experiments I have described because this is an ontogenetic study, and I had first to master the most primitive stages. The later stage of written language is much more complicated, much more puzzling.

*Magoun:* The generalizations that you found here do not necessarily apply when you come to the study of written symbols?

*Luria:* No, because written language is developed on the basis of a ready-made spoken language, and the words are quite different (25).

*Magoun:* Might I go one step further still, and ask whether the generalizations you draw from your work on the beginnings of language in the infant are applicable to or different from conclusions drawn from the study of aphasia?

*Luria:* My book on rehabilitation of functions (27) will soon appear in English, and the book on aphasia (26) will also appear in English.

I don't like to generalize from the early stages to pathology. Too many mistakes are made by generalization because, in pathology, there is a deficit which has nothing to do with the developmental stages but which depends on what part of the brain has failed or been destroyed.

*Keller:* I have a question. You did not intend to place any particular emphasis on the age of the child, as an age group, did you?

*Luria:* You are right. This age of 3 or 4 is just the general range. But it is interesting that we find a decisive turning point in all our experiments between the ages of 4 and 5 years. Something very important happens in the human being in this period. It is the period when speech is interiorized, when voluntary movements are developed and performed, and I think there must be some very intimate relation to maturation.

G. I. Poliakov in Moscow, one of the very great experts in the maturation of the brain, thinks that perhaps it is only in man that there is this period of growth of the connections of the frontal lobes and the feedback systems. A child of 4½ or 5 years begins to organize his behavior without external reinforcement, which means, perhaps, that by then a system of internal feedback has been developed. Isn't it so, Dr. Pribram, that this period coincides with the period of maturation of this last component of the total system?

*Pribram:* I can't answer that now, but we are currently doing experiments designed to give information on this point.

*Fremont-Smith:* Professor Luria, you spoke of the age when voluntary movement begins, but you use the term *voluntary movement*, differently from the way we do, and I think it would be helpful to us if you would explain your use of the term.

*Luria:* I had in mind only the complex forms of voluntary movement which are made when the child obeys generalized rules of behavior.

*Fremont-Smith:* In response to a command?

*Luria:* In response to its own command. I was speaking of complex forms of voluntary movement.

*Fremont-Smith:* Commands which always previously came from the outside world?

*Luria:* Yes, and then became interiorized.

*Lowell:* We find, in postmeningitic hearing losses, that the critical period for the retention of previously acquired language and speech patterns seems to be a little earlier, at 3 or 3½ years of age. There appears to be a critical period at about this time. If a child loses his hearing after this age, he is more likely to retain the speech patterns that he had acquired through hearing. If he loses it before this time, speech generally deteriorates markedly.

*Luria:* It does not have to do with the regulatory function of speech.

*Lowell:* This sort of evidence for a critical period would not be inconsistent with Professor Poliakov's findings.

*Luria:* I have used my time so far to show the members of this conference that the process of development of behavior is a very complicated and a very dramatic event. I want to point out that any real approach to these developmental problems must be a dialectic one. As quantitative changes appear in development, new systems with new issues are built up. A social level of organizational behavior via speech control is formed in the process of behavior, with changes at different levels. Initially the self-regulatory influence of speech is very weak and does not play any decisive role in the organization of these processes, but in the later stages of behavior, it becomes a potent organizing factor. In order to understand the specificity of the development of human behavior or the interaction of the two signaling systems, as Pavlov (30) called them, one must trace this dramatic history of the developmental stages. That was the essence of what I have tried to present.

The subject of the remainder of my talk will concern material on the pathological states of the brain, and I shall start directly by demonstrating some experimental findings in an attempt to show how far the same methods with the same components of the controlling role of verbal activity can be used in their elucidation.

It is often assumed that pathological states are merely a dissolution, a process that is the reverse of development. This is not true. The structure of the pathological process depends on the type of lesion, and there are at least two general types of pathological states which can be expressed by the indicators I use. *Type A* is when the lowest levels are disturbed but the highest levels with speech control are preserved, and *Type B* is when the lowest levels are the better preserved and the highest levels are disturbed. Both types are found in pathology. Unless this essential point is grasped, there can be no access to a good clinical analysis of behavioral changes.

Parkinsonism is an example of a state in which the lower levels of the brain are disturbed though the higher cortical level can be preserved within limits. This is a very good example of the pathology *Type A.*

Pathological disturbance in the lowest level of behavior can be observed, but some compensation can be introduced by cortical activity.

Figure 171 is the record of a medical student with the Parkinsonian syndrome, whom I observed 35 years ago. When, for example, this patient was asked to press the balloon many times, the record showed the blocking of voluntary movements that is a common symptom of Parkinson patients; they begin to move and then suddenly there is hypertension of muscles and tremor and they can't move any more.

The problem is whether some compensation for the defect can be obtained from high cortical levels. Neurologists know that the Parkinson patient who cannot spontaneously take five or six steps can sometimes climb a staircase very well. This is because, in the case of the staircase, every stair gives a signal and the simple synergistic movement from the level of the basal ganglia becomes a movement organized via cortical feedback.

Now, we came to the question: Could we use the same cortical device to overcome this blocking of movement? I used blinking. I told the patient, "Blink and every blink will be a feedback signal for you. Blink and press, blink and press." The result is shown in Figure 171. He blinked and pressed, blinked and pressed. The movements were organized via cortical regulation.

Another example is shown in Figure 172. At first, the patient pressed, but soon the tremor made it impossible. I then said, "Count to 8, but don't use your tongue; use your hand." The movements were restored because they were now included in a new functional system, a verbal functional system and this cortical level was unimpaired in this patient.

Figure 173 is another example of spontaneous movements. The patient could not make any spontaneous movement without developing

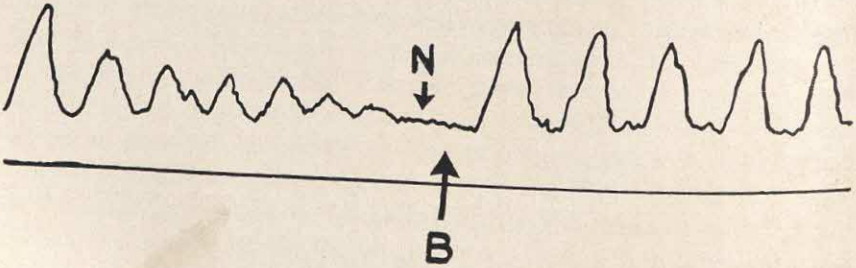

FIGURE 171. Rhythmic movement of the wrist on instruction, in a case of Parkinsonism (B. R.). At "N" the patient said he could not go on. At "B" he was instructed to blink and move his wrist. Reinforcement by feedback from associated blink restored ability to flex wrist.

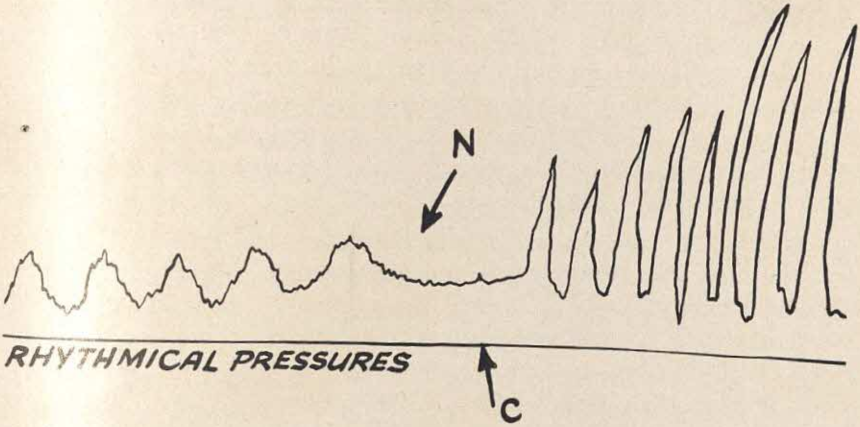

FIGURE 172. The same patient as in Figure 171 (B. R.). Verbal counting restored and augmented his wrist movements. At "N" he said he could not go on. At "C" he was instructed to count.

muscular hypertension. I said, "Tell me how many wheels are there on an automobile? But tell me with your fingers, not with your tongue." He indicated, 1, 2, 3, 4. I asked him, "How many points has a red star?" He indicated, 1, 2, 3, 4, 5. If I included the movement of the patient in a cortical-verbal system, I could overcome his difficulties.

*Doty:* What about the fatigability of this effect? Can this be done repeatedly?

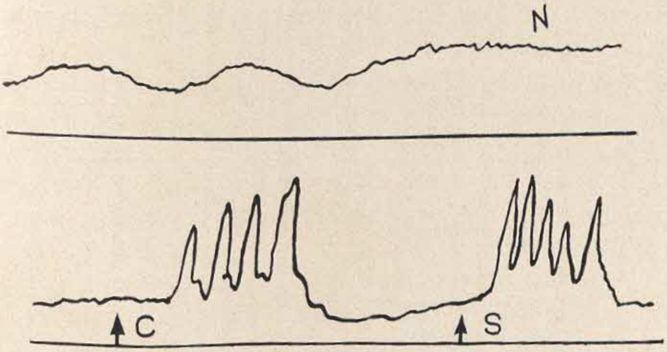

FIGURE 173. The same patient as in Figure 171 (B. R.). The patient, although unable to press without reinforcement, responded correctly when indicating counting. At "N" in the upper record, the patient said he could not go on. At "C" in the lower record, he was asked to indicate the number of wheels on a car, and at "S" the number of points on a star.

*Luria:* No, it has limits. This is only a model. It has nothing to do with treatment as such. But the same patient had used a special device that he himself had invented to improve his speech. He fastened a device on his mouth which gave him feedback signals and, as a result, he spoke better. This lead needs to be elaborated and developed. This is only the general principle, and from a general principle to practical work is sometimes a very long distance.

*Livingston:* I was indeed greatly impressed by Professor Sokolov's disclosure of the definitiveness and character of the neuronal model that he has discussed. It seemed to me that an even more general characterization of neuronal activity in terms of brain circuitry could be drawn to involve the motor systems (the motor analyzers) as well as the sensory analyzers. Perhaps each motor activity that we undertake leaves a residue approximating a model of that activity which would become strengthened with each repetition of the act. It could become, not only more definitively established, but also reduced in the extent of the neuronal circuits involved in the model. Thus, the first attempts at movement seem to involve a great many regions of the brain, and later, when that movement becomes systematized and becomes a habit, the brain areas apparently involved in the act become very much reduced in extent.

Yet, after a motor performance has become well established, if you now try to modify that movement even in a slight respect, immediately, this novelty seems to bring about a reactivation of vaster, less discretely organized regions of the brain (which had been left out of this system as the specialized neuronal model of the performance had been initially perfected).

I think such an introduction of novelty into motor acts may be considered analogous to Professor Sokolov's notion of novelty on the sensory side. Perhaps there is an analogue to the orienting reflex associated with the motor systems which can bring into activity vast regions of the brain. I am suggesting that the motor and sensory neuronal systems may perform in closely analogous ways, and further that an exploration of this notion might reveal that neuronal mechanisms for these parallel functions might be shared. To me, it would seem possible that a similar if not perhaps the same mechanism may offset both the upstream and the downstream sides of the nervous system in both the sensory and motor spheres.

*Luria:* Yes, you are quite right. We both agree, I think.

*Sokolov:* I agree with the remarks of Dr. Livingston, because this problem is of very great importance. I can describe some experiments that were made in a study of the influence of these changes of the motor system on the orienting reflex. The experiments were conducted as follows: The subject, with some effort, had to lift a weight with his finger. This movement was repeated, and the EMG was recorded. Then, we changed the proprioceptive stimulation by changing the weight. The remarkable result was that when we made this weight lighter, instead of a decrease in the EMG activity, there was an increase.

A special adjustment had been elaborated by the nervous system to produce a certain degree of muscle tension, and the unexpected decrease of weight, within certain limits, produced the increase in the EMG at the same time that vascular and EEG reactions were noted.

This means that the same rules that can be formulated for sound or light stimulation are applicable to the motor system. In fact, in a conditional reflex, we have a model which consists, not only of the sensory part, but combines the stimulation, the reaction, and the reinforcement. If either the stimulation or the sensory reinforcement is changed, the orienting reaction results.

We can change the reaction by changing the degree of tension produced, and this evokes the orienting reflex. Or we can change the reinforcement; instead of one intensity, we can use another. For example, suppose we produce a defensive reflex with a reinforcement of, perhaps, 9 units of electric shock. A defense reflex becomes elaborated. Then, if instead of 9 units, 12 units or more are used, there is an intensification of the orienting reaction instead of an increase of the defensive reflex. I agree completely that this can be analyzed from this point of view.

*Luria:* In the case of Parkinson's disease, the cortex is often preserved and at least within limits it can be used as a device for compensating for defects at the subcortical level. But this same principle can be observed even in pathological states of the cortex. There are some pathological states of cortical deficit in which it is possible to reorganize and compensate for the defective cortical processes by introducing the speech system.

The next experiments (Figures 174 and 175) show data on two children who are not feeble-minded but who have cerebral asthenia. By cerebral asthenia I mean weakness of the cortex caused by, for example, toxic conditions or by alimentary dystrophia or by trauma and so on. This is a chronic asthenia which can last for several months but which is curable and reversible. It can be shown, in these cases, that the highest

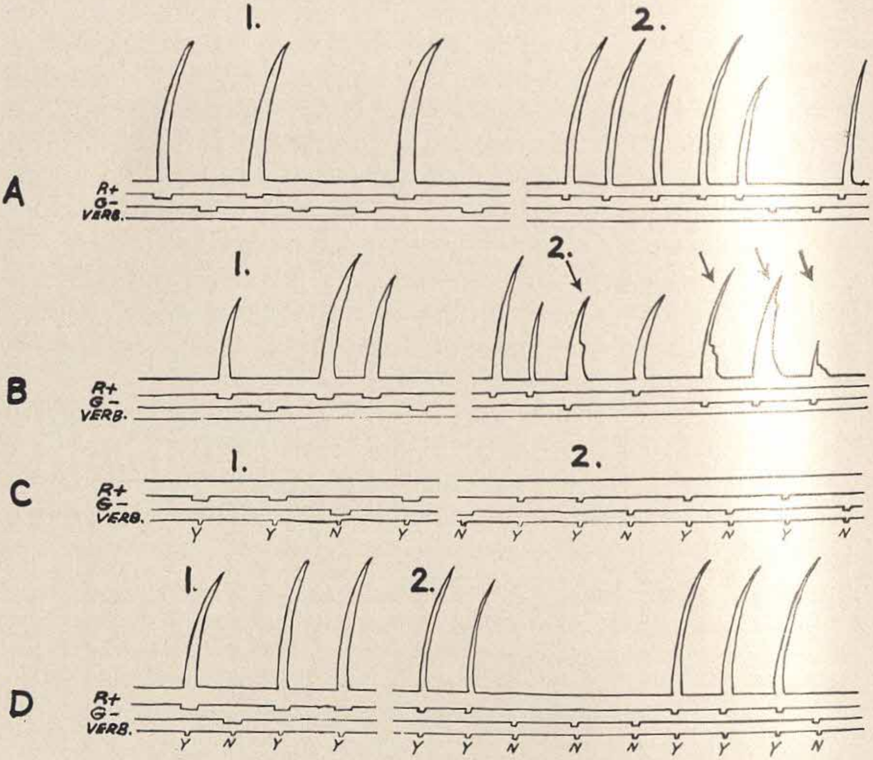

FIGURE 174. The regulating influence of speech in children of school age. Traces same as in Figure 165 (*B*). (*A*) Normal 9-year-old child instructed to press on red (R+) only. 1st regimen (1.): long-duration signals, long intervals. No errors. 2nd regimen (2.): short-duration signals, short intervals. No errors. (*B*) Child (10 yr.) with cerebral asthenia. After instruction to press on red (R+) but without his own verbal reinforcement. Errors (arrows) in the 2nd regimen. (*C*) Same child instructed to respond verbally. "Yes" for red (R+) and, "No" for green (G−). No errors. (*D*) Same child instructed to give both motor and verbal reactions. No errors. (From the work of E. D. Homskaya)

level of organization via speech is preserved. This method can thus be used for functional compensating defects.

Figure 174 *A* shows results of an experiment of Homskaya in a normal child of 9 years. The red light is a positive and the green light a negative stimulus. The child has to press on the red, withhold on the green. On the left, in the first regimen of tests with long stimuli and long intervals, there are no failures. In the second regimen of tests (on the right), in which the signal is very short and the intervals between signals also short, he can still function accurately. But a child

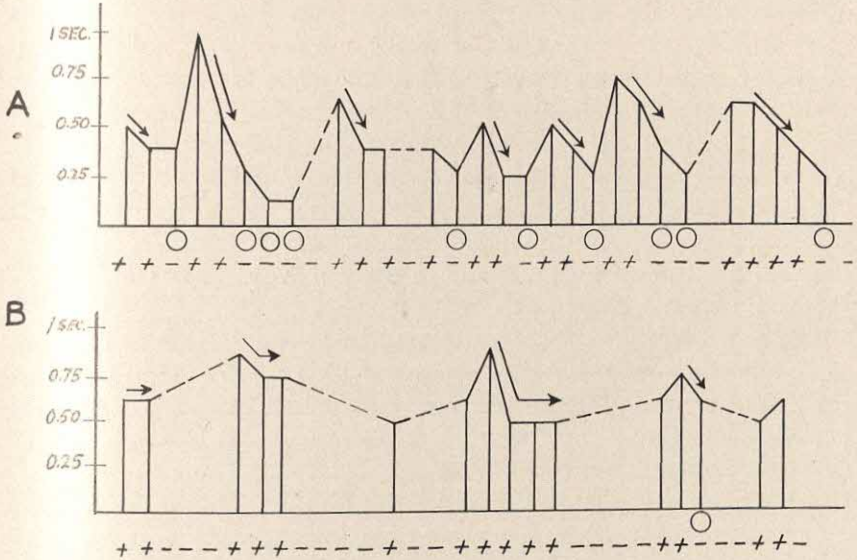

FIGURE 175. Reaction times of motor responses in a child with cerebral asthenia, excited type (P., 10 yr.). The bottom line indicates signals. Plus = red light (press) and minus = green light (do not press). Errors are marked by circles. (*A*) Motor reactions without verbalization. (*B*) Combined motor and verbal reactions.

with cerebral asthenia gives a different picture. The cerebral asthenic child reacts positively to positive stimuli, but there are disinhibitions of reactions to the negative stimuli, for he does not withhold his response. When the green light is given in quick repetition, the child presses and says, "Oh, I made a mistake." He cannot withhold; he cannot inhibit his movements. That is the pathological state that must be overcome (Figure 174 *B*).

So the same method is used but the child, instead of pressing, is now allowed to answer "Yes" to a red light and "No" to a green light. He verbalizes correctly, even with the second regimen in which the stimuli are short and quickly repeated (Figure 174 *C*).

Then both tests are combined. The child is instructed to answer "Yes" on the red light and press, and to answer "No" and refrain from pressing on the green light. This involves the feedback action of the child's own speech, and in this case, there are no mistakes. Instead of the 50 or 60 per cent mistakes that occurred in the experiment without verbal control, there are none in the series with control (Figure 174 *D*).

The second example of the same phenomenon observed by Homskaya is shown in Figure 175. The child makes many mistakes, as indicated by the arrows in the series without speech, but none with verbal control. The second time speech is omitted, there are again mistakes.

What are the mechanisms of this phenomenon? We are only at the start of this work, but I am very sure that the real mechanisms of this compensatory action are changes in the orienting activity which were provoked via the child's own speech. By adding the child's own verbal reaction, we raise the activity of the cortex in a specific way and stabilize the connections involved in this behavior. We reinforce the processes of active inhibition.

Figure 175 *A* shows the latent period for every reaction in the series of results without speech. A positive stimulus gives a latent period of reaction of 85 seconds. The next positive stimulus gives a shorter latent period of reaction. Then, when a negative stimulus is given and the child gives a disinhibited reaction, he fails to refrain from pressing. The trend to shorten the latent periods brings on the disinhibitory reaction.

When the same series is repeated but accompanied by speech, the latent periods are longer and there is not the same trend toward quicker and quicker responses. Speech reinforces the inhibitory activity of the cortex. That is one of the mechanisms of the controlling function of verbal reactions in this case.

Figure 176 illustrates the reverse situation from that shown in Figure 175. There is another class of cerebral asthenic children in whom the inhibitory components are dominant. If the same stimuli are given in the first regimen, long signals with long intervals, the child does all right, but with short and rapidly repeated stimuli, the inhibited child cannot follow, and he leaves out reactions to positive stimuli. That is another type of pathology. In the first type, there was a defect of the disinhibitory process, and in the second type, there was the defect of the excitatory process. The children in the first group are restless when they are in a state of fatigue, but those in the second group are torpid when fatigued.

If I combine the motor and verbal reactions, the child does not only make mistakes, and there are even instances of disinhibition of reaction which were not seen at all in the first experiment. Figure 177, which also is the work of my collaborator, Homskaya, illustrates the reverse tendency. The latency of reaction to the first positive stimulus was about 60 seconds; to the second, 1.30 seconds or more; on the third positive stimulus, there is no reaction at all. This is a process of gradual inhibition of reaction.

In Figure 178, a combination of verbal and motor reactions is given

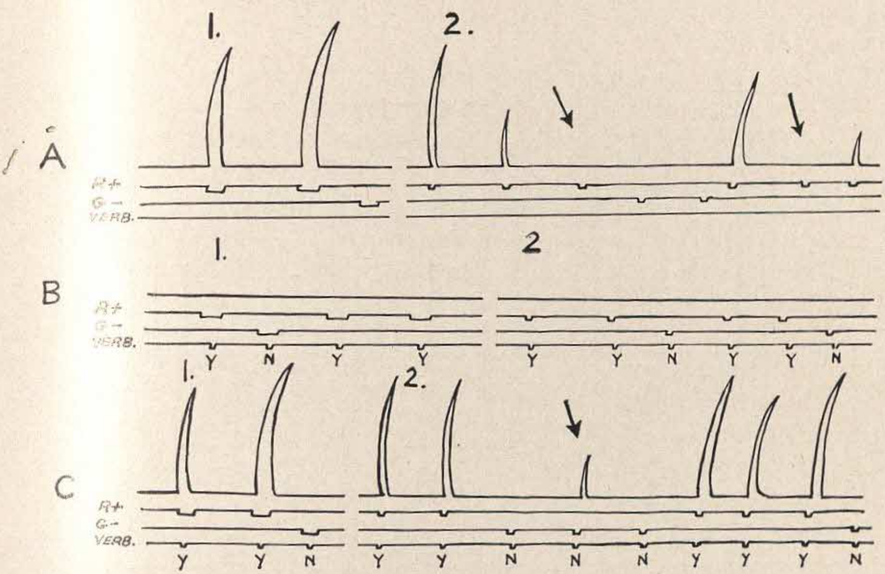

FIGURE 176. Child (N. E., 9 yr.) with cerebral asthenia, inhibited type. Traces same as in Figure 165 (*B*). (*A*) Instructed to press only to red (R+) and to refrain on green (G—). Some errors to positive stimulus (arrows). (*B*) Instructed to say "Yes" (Y) to red, "No" to green. No errors. (*C*) Combined motor and verbal reactions. The signal error (arrow) is disinhibition to negative stimulus.

and there is a normalization of the process. The latent periods are shorter and there is no tendency to irradiation of inhibitory processes. It is very important that such a regulatory influence of speech occurs only when the speech is semantically meaningful. If the child is instructed, "Press every time, and just say, 'I see, I see, I see,' " in positive and in negative cases, there is no normalizing effect (Figure 178). If instead the child says, "Yes," for positive and "No" for negative, the result is all right, for the speech has a semantic sense. Only a differential, meaningful speech has an organizing effect.

Figure 179 shows the organization of the movement itself that verbal activity can bring. The experiment is as follows: The child is told to press *strongly* on the red light, *gently* on the green. A normal child does this very well. But, in the second regimen (of short quickly repeated stimuli), there is a gradually diminishing curve. The shifting from the positive to the negative signal does not evoke a rapid change of organization from the strong to the gentle reaction. But if speech is combined with motor reaction in the same experiment, the resultant process is very

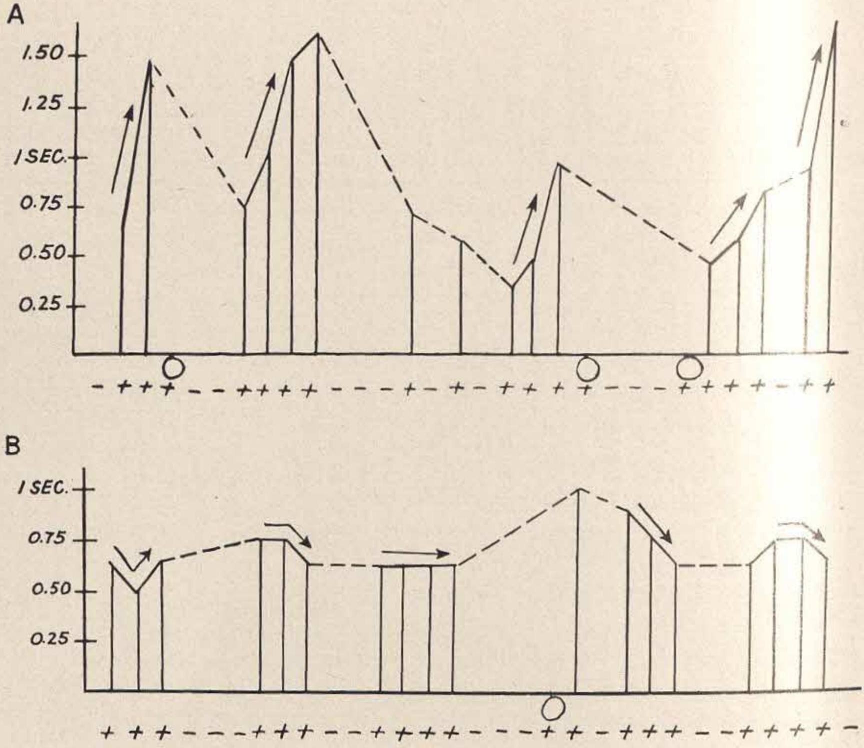

FIGURE 177. Reaction times in a child with cerebral asthenia, inhibited type (same child as shown in Figure 176, N. E., 9 yr.). The bottom line indicates signals. Plus = red light (press) and minus = green light (do not press). Errors marked by circles. (*A*) Motor reactions without verbalization. (*B*) Combined motor and verbal reactions.

mobile and the reaction quickly changes from strong to gentle. This is an important example of the regulative role of speech even in the control of differential motor responses.

These are all results from patients of *Type A.* This group has pathology in that the more primitive processes are disturbed; however, the higher levels are preserved, and there is a possibility of compensation through speech. There is another very large group that shows pathology, *i.e.*, *Type B*, which are the cases in whom both levels are disturbed, the highest levels being even more disturbed than the lower ones. In this category are the oligophrenic (feeble-minded) children, children who have suffered severe brain disease in the intra-uterine periods, in the moment of delivery, or in the first months and years of their lives.

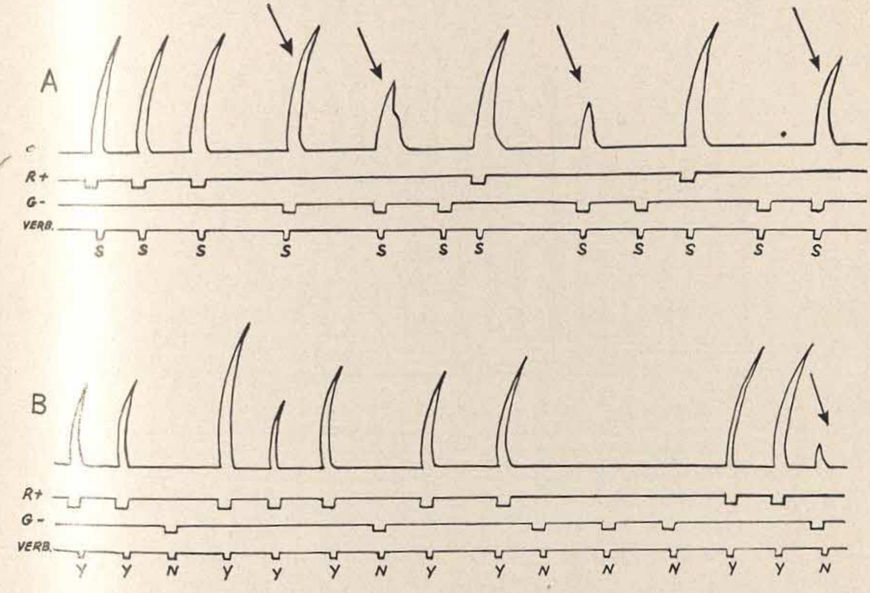

FIGURE 178. Combined verbal and motor reactions in a child (G., 11 yr). Identification of the traces is the same as in the legend for Figure 165 (*B*). (*A*) Instructions were to give nonspecific verbal expression ["I see" (S)]. Note errors marked by arrows. (*B*) Instructions were to give specific verbal reaction with semantic meaning ["yes" (Y) for red light (R+) and "no" (N) for green light (G—).] There is only one error (arrow) when the verbal reaction is specific.

In these children, it is characteristic to find both levels disturbed. For example, an imbecile child was instructed to press when given a signal (Figure 180). As can be seen, this imbecile child of 12 gave an irradiation of superfluous movements which he could not stop; this is very similar to what is found in the 2-year-old normal child.

Figure 181 shows responses obtained from an imbecile who gave a very stereotyped reaction. When the child was told, "Press on the short signal; do not press on the long," he pressed the first time, refrained the second, but then continued to alternate irrespective of the signal. His response had become completely stereotyped. I cannot use the method of autoreinforcement of the child via his own speech in this case because there is a deficit in the speech level of the child as well as in his motor level. In Figure 182, the child had only to press, to make movements at every signal, but it was a motor stereotype which was very characteristic for this imbecile child. When the same child was instructed to answer verbally every time there was a signal, the verbal

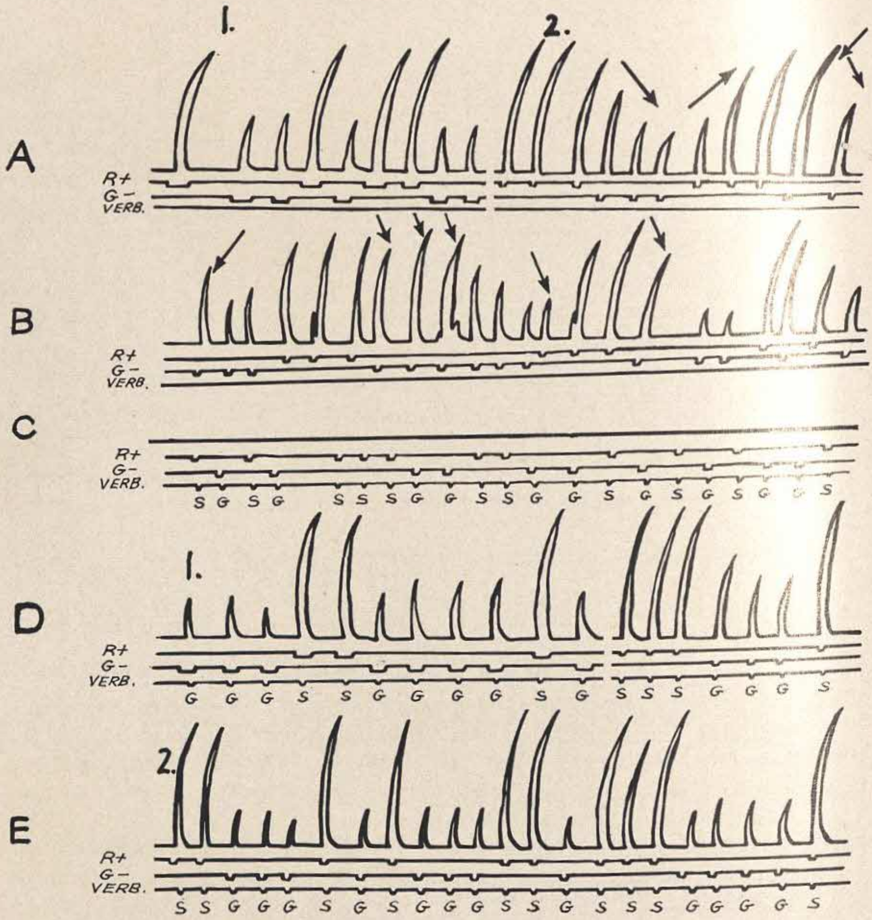

FIGURE 179. The regulating influence of speech in differentiating by motor reactions in a child with cerebral asthenia after head trauma (D., 9 yr.). The child was instructed to press strongly on a red light (R+) and gently on a green light (G—). Identification of traces is the same as in the legend for Figure 165 (*B*). (*A*) Without accompanying speech, a gradual change developed. Arrows indicate errors. (*B*) Continuation of same record. (*C*) The same instructions, but to verbalize only. S = "strong," G = "gently." No errors. (*D*) Combined verbal and motor reactions (1st regimen). No errors. (*E*) Combined verbal and motor reactions (2nd regimen). No errors.

reaction showed the same stereotyped character as the motor reaction of the hand (Figure 183).

In many cases, the verbal reactions are even poorer than the hand reactions. Figure 184 gives responses obtained from an imbecile child

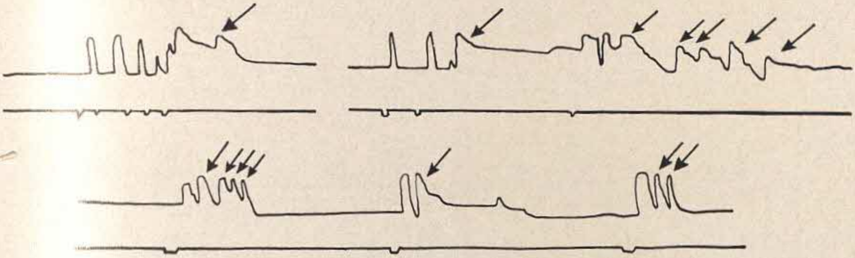

FIGURE 180. Motor reactions to light signals (notched line), in a 12-year-old child (B. S.) who was instructed to press only on the signal. Arrows indicate erroneous perseveration of responses.

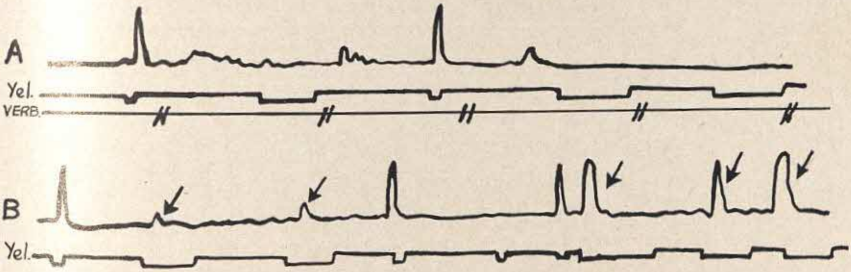

FIGURE 181. The instability and disappearance of well-differentiated responses of a 12-year-old imbecile child (S.) when the reinforcing verbal praise for accuracy was removed. The signal was always a yellow light (Yel.), but the child was instructed to press only when the signal was short and to refrain when it was long. (*A*) After several trials, a stage was reached at which no errors were made when the response was reinforced by the experimenter's saying, "Good" [indicated by the hatched signal line (Verb.)]. (*B*) Without this reinforcement, many errors were made (arrows).

of 14. The instruction was to press on the third signal but to withhold on the first and second. Withhold on the first and second of the next time, express on the third (minus, minus, plus; minus, minus, plus). After many trials, this child did quite well with his hand activity, but when I replaced the hand activity by a verbal reaction, he failed. The child was told to say, "No, no, yes; no, no, yes." The figure shows that there was a gradual irradiation of response, the child adding more and more "no's" each time. Speech could not be used as a regulating device in this case because the speech level itself was disturbed.

Responses shown in Figure 185 are those of an imbecile child of 10, who was trained to give quite good differential reactions, positive reactions to one signal and negative to the other. But in this case, if the

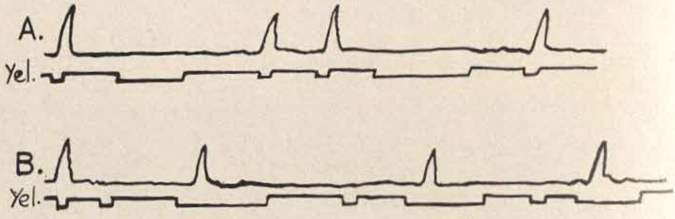

FIGURE 182. Conversion of an appropriate response to a meaningless stereotyped one in a 10-year-old oligo-schizophrenic child (S. X.). The signal was a yellow light (Yel.), and instructions were to press when the signal was short and to refrain when it was long. (*A*) When asked what he did, the child answered, "On the short, I pressed; on the long, I didn't." No errors. (*B*) Continuation of the same test. A stereotyped alternation of pressing and withholding developed but, when asked what he did, he gave the same answer as before, *i.e.*, he had a false recall.

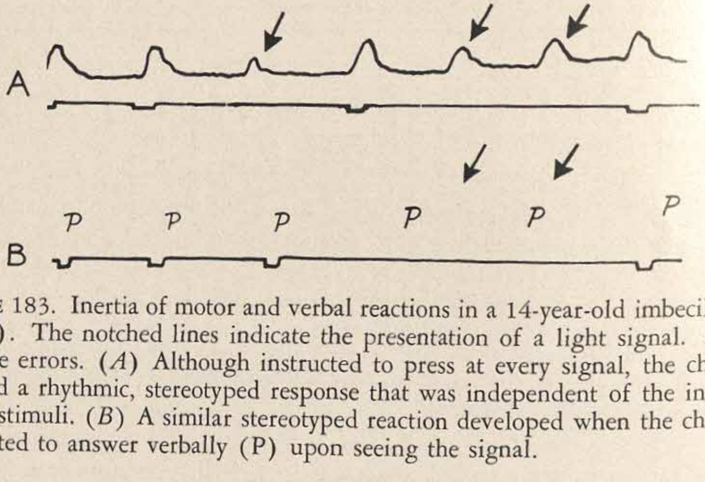

FIGURE 183. Inertia of motor and verbal reactions in a 14-year-old imbecile child (L. F.). The notched lines indicate the presentation of a light signal. Arrows indicate errors. (*A*) Although instructed to press at every signal, the child developed a rhythmic, stereotyped response that was independent of the incidence of the stimuli. (*B*) A similar stereotyped reaction developed when the child was instructed to answer verbally (P) upon seeing the signal.

motor reactions were combined with speech, the result was worse. He said, "No," but he pressed. In this child, speech brought a disorganization of behavior because speech itself was a disturbed function.

Figure 186 illustrates responses of an imbecile child of 14 with good elaborative action without speech. But when his own speech was introduced, he reacted like a normal child of 3. The impulse to speak had a disinhibitory influence.

I shall now pass to some experiments that are currently in progress and have not yet been published. This is material from our neurosurgical clinic, from patients with local lesions of the brain. The problem is this: Are there different systems in the brain cortex which

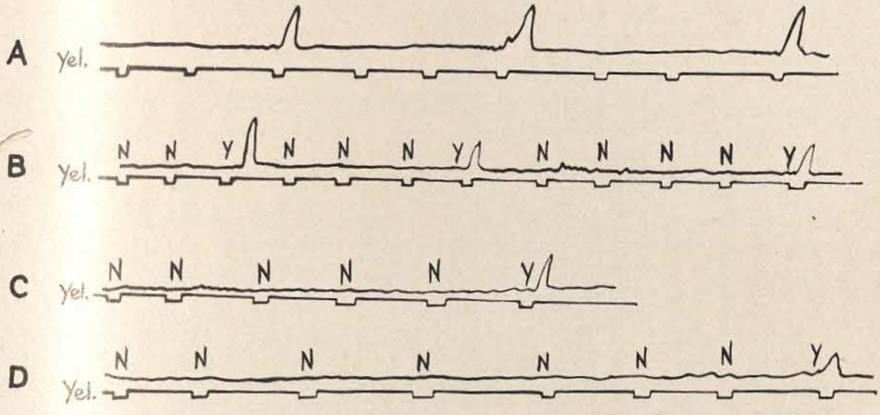

FIGURE 184. Pathological inertia of verbal reactions in a 14-year-old low-grade imbecile (B. R.). The signal was always a yellow light (Yel.), and the instruction was to press on every third signal. (*A*) After long training, the child learned to do this correctly. (*B*), (*C*), and (*D*) When asked to verbalize (no, no yes, no, no, yes) simultaneously with the motor pattern, the child at first succeeded but gradually made more and more errors until the negative responses increased in number, indicating irradiation of inhibition. Y = yes; N = no.

have different functions according to the Type A and Type B of our model? I want to present data to show that in the human brain there are regions which, after disturbance, give results like those of Type A, and there are other regions which, after disturbance, give results like those of Type B.

Figure 187 gives data from the experiments of Homskaya. The patient had a *parietal lesion*, and in this case he was instructed to press strongly when he saw a red light and gently on a green light. He made many mistakes, and his movements were disorganized, but when I instructed him to give his own commands, which have a feedback influence, the whole process was changed. When he said, "Strong," he pressed strongly, and when he said, "Weakly," he pressed weakly.

*Lilly:* Are these bilateral lesions in this series of patients?

*Luria:* These can be bilateral lesions or lesions of the dominant hemisphere. In this case, the verbal system can play a compensatory role for the local brain injury. It is well known that the patient with a precise limited lesion in one of the posterior intrinsic zones (parietal, occipital, or temporal) can compensate for the deficit by a kind of verbal organization of his behavior. Note, for example, the patient with visual agnosia who can use the whole semantic system, which is pre-

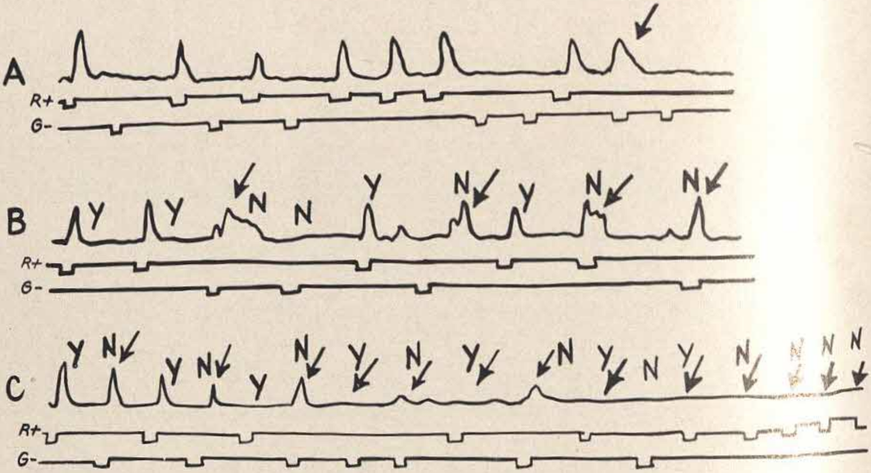

FIGURE 185. Failure to obtain good regulation by verbal influence in a 10-year-old imbecile child (V. B.). (*A*) Motor reactions to instructions to press on a red signal (R+) and to refrain on green (G—). After three or four training sessions, the child made only one error (arrow). (*B*) and (*C*) When asked to verbalize as well, saying yes to red and no to green, many errors (arrows) were made. At signals in (*B*), there is disinhibition; he said, "No," correctly, but his motor response was disinhibited. In (*C*), his verbal response was a stereotyped alternation of yes and no, and inhibition became irradiated from the motor to the verbal sphere. Y = yes; N = no. (From the work of O. K. Tikhomirov)

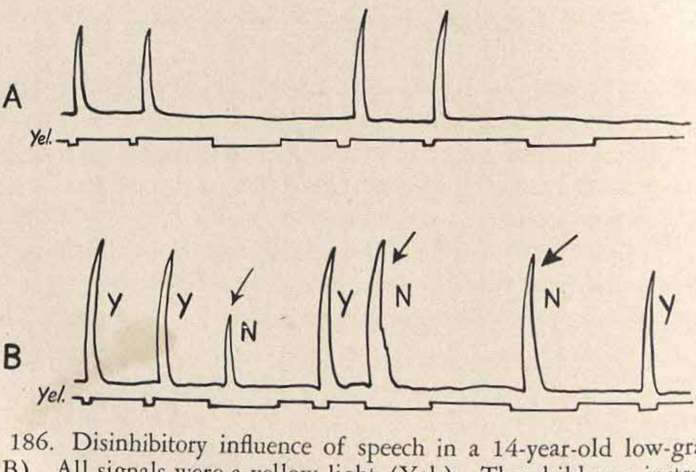

FIGURE 186. Disinhibitory influence of speech in a 14-year-old low-grade imbecile (B). All signals were a yellow light (Yel.). The child was instructed to press only when the signal was short and to refrain when it was long. (*A*) After several days of training, he learned to do this correctly. (*B*) When asked to verbalize simultaneously, he failed (arrows) to inhibit motor reaction on long signals even though his verbal response was correct. Y = yes; N = no.

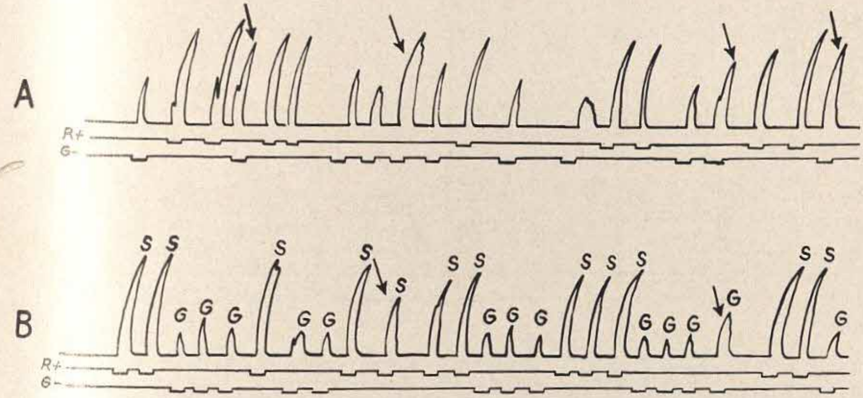

FIGURE 187. Regulating influence of speech in elaborating differentiations in motor reactions. The 47-year-old patient (K.) had a lesion of the left parietal lobe. Instructions were to press strongly on the red light (R+) and gently on the green (G—). (*A*) Motor reactions without verbalization. Many errors (arrows). Almost complete failure to follow. (*B*) With verbalization. Only two partial errors (arrows). S = strong; G = gently.

served, for reorganization of functions and for compensation of the deficit. Reorganization of function based on the second signaling system is a general means for retraining these patients.

*Brazier:* Professor Luria, would you find that result with a dominant hemisphere lesion?

*Luria:* If the lesion on the dominant side is partial, and not total, it can be done.

*Pribram:* But aren't these parietal, not temporal lesions? There is no auditory involvement there.

*Luria:* It is parietal, yes. But if there were a speech defect, that would be a complicated case, and that is why I choose the patients with good speech but poor motor organization.

*Bodian:* Could you show us the position and the size of the lesion, perhaps, in a simple way?

*Luria:* This report represents, not one patient, but many different ones.

*Keller:* Are these total parietal lobectomies?

*Luria:* No, they are partial lobectomies. If we pass now to patients with well preserved movements and well preserved speech but with frontal lobe lesions, we find a different picture. Figure 188 shows the findings on two patients, one with a right frontal lobe tumor and the other with a left frontal lobe tumor. The instruction given is to press

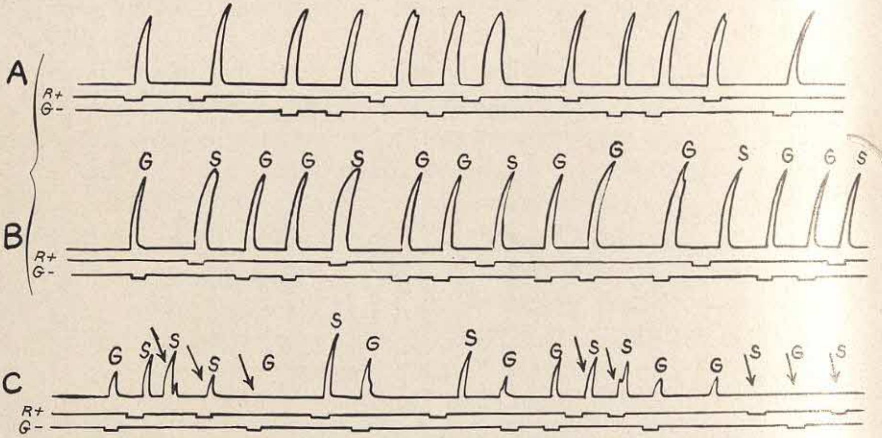

FIGURE 188. Patients with tumors of frontal lobes; given same instructions as those in Figure 187. (*A*) 50-year-old patient (V.) with tumor of left frontal lobe; without verbalization. All motor reactions were of equal strength. (*B*) Same patient as in (*A*); with verbalization by the patient. All motor reactions were of equal strength although some were of longer duration than others. Verbal responses are correct. (*C*) 52-year-old patient (K. Z.) with a tumor of the right frontal lobe. With verbalization, many errors (arrows) and extra responses are made. Inhibition irradiates and finally becomes general. S = strong; G = gently.

strongly on the red light and gently on the green light. There is no difference; these patients press equally to both lights.

*Pribram:* Do these patients still have the tumor or have they been operated upon?

*Luria:* This is after removal. At the next stage of the test, the same patient is told to combine the motor reaction with a verbal reaction. He has to say, "Gently," to the green light and "Strong" to the red and to press according to the instruction. The verbal reaction, as Homskaya (15) has shown, is of no help to these patients. They press equally intensely on both signals.

*Windle:* How different are the two words in Russian? One is not necessarily a very short, one-syllable word, and the other a long word?

*Luria: Silno* is "strong" and *Slabo* is "weak." Each has two syllables. But the same result is obtained by the use of other words that have the same meaning. The verbal answers are all right, but they have no regulating role. The patient says, "I shall press gently," but he presses just as hard as he pressed before.

With deficits of the frontal lobe, there is no feedback from the patient's speech, and no organization and regulation of behavior as a result of verbalization. The same thing can be demonstrated by a different technique. First, let us take the case of lesions which interrupt the connections in the system of the premotor cortex and subcortical ganglia. Figure 189 shows reactions of a patient who had a hemorrhage after an exploratory operation of the premotor zone. When he was instructed to draw a circle, he drew a circle but he could not stop. When told to draw a square, he started with a square but changed into a circle. On being asked to write "122," he wrote 122-2-2-2-, and so on. He could not stop.

Figure 190 shows reactions of a patient with a tumor of the motor region. On the second day after operation, there was postoperative edema which disturbed the organization of his behavior. When asked to draw a circle, he drew and drew and could not arrest the movement. When told, "Draw a triangle," he drew a circle twice and he could not stop. This is motor perseveration. On the third postoperative day, there was the same deficit. On the fourth day, he did a little better. He could draw a circle and he could draw a triangle, but with a cross, he

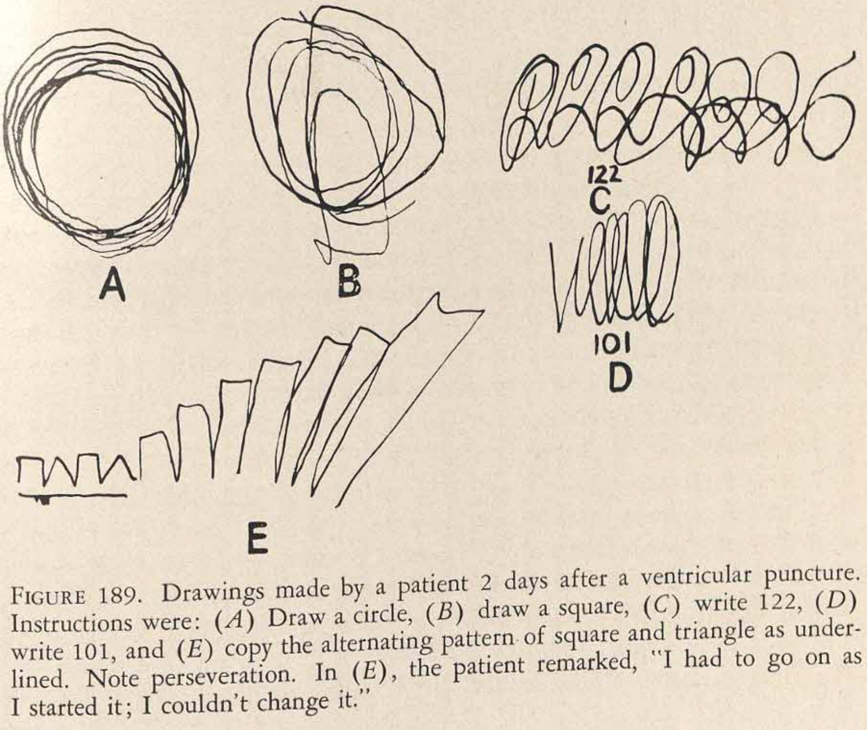

FIGURE 189. Drawings made by a patient 2 days after a ventricular puncture. Instructions were: (*A*) Draw a circle, (*B*) draw a square, (*C*) write 122, (*D*) write 101, and (*E*) copy the alternating pattern of square and triangle as underlined. Note perseveration. In (*E*), the patient remarked, "I had to go on as I started it; I couldn't change it."

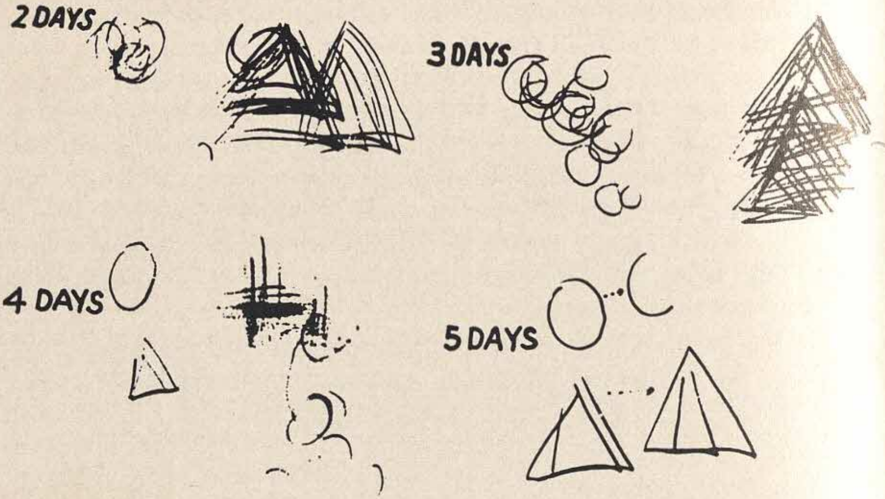

FIGURE 190. Drawings of circles and triangles, made by patient (E.) on different days after operation on left premotor region (2, 3, 4, and 5 days postoperatively).

was exhausted. He had become exhausted and perseveration began. On the fifth day after operation, his performance was quite good, and on the seventh day after operation (not shown in the figure), all was well.

When the same patient was instructed to draw a man, he began to draw a man and accomplished this task quite well. But when he came to draw the legs of the man, perseveration began. He drew many, many legs, and could not stop. He said, "I know that there are too many legs but I can't stop. Let him walk a little." The same was observed on the third day after operation and on the fourth day, but by the fifth day, the motor perseveration had gone and the patient did well. This is a functional method of studying edema. We have developed a technique or functional proof of the intensity and topical spreading of edema. A paper devoted to this topic has been written by Spirin (32).

The defects are quite different in patients with lesions of the prefrontal lobes. It is interesting that these patients cannot even obey a verbal instruction. Not only the motor component of the behavior is disturbed, but even the semantic, the attitudes, the content of behavior. When the patient is told to write his name, he signs. But when this is followed by a request to write the letter "A," he again signs his name. He is then asked to draw a circle, but he signs his name once again. He cannot shift from one type of activity to the other. This is not a motor perseveration (Figure 191).

*Sokolov:* But he is conscious of his mistakes.

*Luria:* He is only half conscious of his mistakes, for there is a very great disturbance of consciousness in these patients, resulting in perseveration of the same type of action.

*Sokolov:* But the understanding of your command is preserved.

*Luria:* Yes, these patients understand the instructions and they can even repeat them. "What did I tell you to do?" "You told me to draw a circle." But when I say to one of them, "Please draw a circle," he writes his name instead. It is a stereotyped reaction that he cannot change.

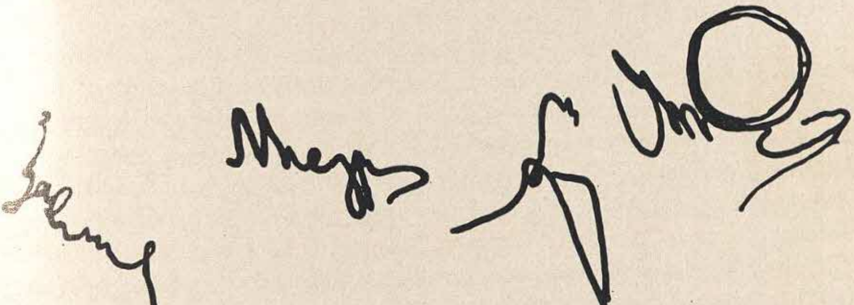

FIGURE 191. Drawings made by a 45-year-old patient (M.) with intracerebral tumor (left frontal lobe). Left to right, upper row: Instructions were, "Sign your name; write the letter A; draw a circle; copy the circle I have drawn." Left to right, lower row: Instructions were, "Copy the cross I have made; draw a circle; trace the cross I have made."

*Sokolov:* Does this perseveration appear only in the case where some repetition of the same command has been made? Or can it follow a single reaction?

*Luria:* Even if there is only one. If there is some repetition, it is absolute. The inertia of this system is so great that even one act, one reaction, can be quite enough to bring about a stereotyped response.

When one of these patients was instructed to draw a circle, he carried it out all right, also the instruction to sign his name. He drew three circles well, so there were some good reactions. When told to draw five lines, he did so. But when this instruction was followed by the request to draw ten *points*, he drew ten short *lines*. When asked to draw twelve crosses, he drew twelve *lines*. Then when asked for three circles, he drew three *lines*. The semantic model of the word "line" was preserved and perseverated.

*Sokolov:* I believe that this experiment is of great importance, because we know that memory is realized through some cycle of processes. I believe this is a case which demonstrates that the realization of certain images in the brain is done through the programming of certain processes, and very specific ones. It relates only to a certain combination of neural cells, because only a very specialized response is observed.

*Luria:* The second command cannot stop the inertia of the first one. If I ask one of these patients to draw a square, he draws one square. Then if I ask him to draw three squares, he draws one square; then he draws a second and a third. He puts "1" and "2" inside the first square, and "3" in the third, but nothing in the second. Then he pauses, draws another square, and he doesn't stop his activity until the whole sheet is covered with squares.

This is an experiment which I made together with my friend, Zeigarnik (39), a pupil of Kurt Levin. I was having a conversation with her and said, "Have you heard about the pact between two governments? It was announced in the papers." The patient overheard the word, "pact," and wrote "pact"; "pact Number so-and-so." This overheard conversation was enough to provoke new activities and new associations.

Then I said to another psychologist who was standing near the bed, "His behavior resembles that of animals with frontal lobe lesions." The patient heard the word "animals," and wrote, "pact about animal breeding." Everything he heard came into his behavior, but it was not linked behavior, merely associated behavior.

This is just an example of the very interesting unbiased, unlinked, unregulated behavior characteristic of patients with frontal lobe lesions. Some work Homskaya (15) is doing in the Neurosurgical Institute may be of interest. We are studying not only the regulation of voluntary movements, but the regulation of involuntary movements as well, and what we find up to now is that in all cases with posterior lesions, quite good stabilization of orienting reflexes can be obtained via speech or instruction, but this cannot be obtained in patients with frontal lobe lesions. The patient with a lesion in the frontal lobe loses his regulating activity of speech.

*Leese:* Professor Luria, what is the emotional background against which you are giving these directions?

*Luria:* The ordinary frontal lobe syndrome.

*Leese:* Are they cooperative, quiet patients?

*Luria:* Yes.

*Kelly:* The use of speech as a regulatory device for finger motor activity leads one to wonder about the reverse process. Perhaps I am doing what the Rorschachers call "space perception," seeing a white space instead of a black space but, in cases of stuttering where there is a dysrhythmia in the speech, one of the old devices used for giving some alleviation was to press the fingers against each other as each syllable of speech was spoken, and thus get a stabilization of the speech function in the stuttering patient, or sometimes one with accented speech. This, I suppose, is a case where the motor activity operates as a regulator on the speech. I don't know whether or not it would work for semantic speech, but at least it works for motor speech.

*Luria:* You are right; it is another kind of experiment. I have used my type of experiment because the role of speech in regulating the different forms of behavior plays such a decisive role in human development.

*Brazier:* In your experiments with the normal child in which he had to say, "Go," and then make the action, I wondered whether the child, if instructed, say, to blink and then press, would give a better response just from having to make an additional movement?

*Luria:* Yes, I think so, if it is a young child and if the experiments were not on the semantic side but the impulse side. Additional movement would help.

*Brazier:* So this would leave out the verbal element?

*Luria:* At this stage. But in more complicated experiments, it is impossible to leave out the verbal instruction, the semantic side of the word.

*Magoun:* There is a program of study supporting the importance of the auditory feedback in motor speech, and this involves a device by which the patient has earphones and hears what he says; there is some delay in this. I gather that you come quickly to a complete block. I am sure Professor Luria is familiar with this, and doubtless many others here are, too.

*Erikson:* What Professor Luria demonstrates in regard to the regulatory function of speech has important implications for the development of conscience: the internalization of "yes" and "no" and the capacity to develop an inner voice, which gradually becomes silent and finally functions without the awareness that that voice once came from the outside. Thus, what Professor Luria has described as an increased mastery of the environment by speech corresponds to an increased mastery of some aspects of what might be called the inner environment; and I would think that what Piaget calls the "clinical" aspects of an experimental situation (*i.e.*, the spontaneously varied, more individualized aspects of the relationship of experimenter and child) probably would reflect the interplay between the cognitive and the emotional aspects of speech.

*Fremont-Smith:* At what age?

*Erikson:* At 4½ years of age, which is a critical age. This has certain implications for the family structure. It is very important for a child of 4½ years to live in some kind of harmonious family, in which the various people who say "Yes" and "No" to him say it in the same way, with similar intonation, and with similar values behind it. Society, therefore, has to keep its type of family intact, so that it can perform the function of supporting a healthy internalization of values.

*Kelly:* But doesn't this produce something like dogmatism if all members of the family say "Yes" and "No" in unison, together? Does this permit the child to re-evaluate his life?

*Erikson:* I didn't say "unison." I said "harmonious."

*Fremont-Smith:* Isn't one of the functions of socialization, as you have described it and as Professor Luria has, to lay the groundwork so that this 4½-year-old child may become an adequate parent for his or her children in the future?

*Erikson:* May I first say, in response to Dr. Kelly, that what I pointed out has nothing to do with any one particular form of society. All societies must strive for a certain harmony in the environment of the pre-school child, and they must adapt their procedures to the child's capacities. As Professor Luria points out in one of the three papers which we were given to read prior to the conference, when "No" is said too early or in such a form that the child cannot gradually manage the "No," disturbances of the kind which we study in the clinic result. Obviously, Professor Luria did not refer to this intermediate area, because he went from the totally normal to the strictly abnormal. There is a whole area in between, where neurotic disturbances, roughly speaking, originate in faulty qualities and quantities in internalized "yes" and "no" signals.

*Fremont-Smith:* What about the preparation for parenthood?

*Erikson:* To me, the problem in studying behavior is not only that of finding out what one single organism can be made to do in a particular experimental setting but also to see what role a behavior item plays in the whole life cycle. In childhood, the preparation is laid for a human being to become a parent (8). So, again, such monkey experiments as were shown earlier bring up the question of how good a parent that monkey can be after having gone through the experience which was shown. Since I do not know what the monkey will do to his offspring, I (strictly speaking) do not know what happened to the monkey's affection—as a monkey. I know Dr. Harlow is going to investigate this and it will make the experiment more relevant.

*Harlow:* This is one of the real questions; that is, what does it take to turn a monkey into a successful parent? I would not be at all surprised to find that it takes quite a bit of essential mother love.

*Fremont-Smith:* This raises a very interesting and fundamental point: When a culture is changed, whether it is a monkey culture or a human culture, it becomes very important to consider what this change will do to the parental capabilities of the children. I bring this up because it seems to me that these are implications that are important. In many countries of the world, efforts are made deliberately by the society to direct the culture in a certain direction. Frequently, not enough thought is given to what this will do to the parental capabilities of these children when they grow up. In Israel, for example, there have been certain problems that have arisen in the Kibbutzim in this connection.

*Luria:* About 20 years ago, when I was very interested in the works of Coghill, I tried to repeat some experiments on the human fetus, the fetus of 5 months of intra-uterine life which has a possible life of about 5 to 8 minutes. Stimulation of the skin caused a spreading wave of excitation, as Coghill pointed out. But, if I stimulated on the mouth, there was no wave of excitation but a sucking movement.

*Bodian:* I might also add that Davenport Hooker in his experiments (16) concluded that the trigeminal area was one of the first to show responses. Perhaps Dr. Windle could tell us more about this.

*Windle:* The 5-month fetus is capable of responding to stimulation of many regions of the skin. The trigeminal region is well supplied with afferent endings, but so are the hands, feet, and other parts. Cat fetuses show some interesting phenomena. When exposed, with placentas intact and before asphyxiation, a lightly applied stimulation of the face of an early cat fetus leads to a quick avoidance response. Later, at stages in development equivalent to human fetuses of 3 to 5 months, this is replaced by a homolateral response. As asphyxia develops, the same stimulus produces a movement toward the side opposite that stimulated—a reversal has taken place (38). As asphyxiation goes on, stronger stimulation is required, and instead of a discrete response, the reaction spreads to the muscles of the trunk and limbs. Mass reactions are characteristic of fetuses of all species during asphyxia; they become the prevalent form of behavior seen 1 to 5 minutes or more after opening the uterus. With further passage of time, the mass reaction becomes weaker, and finally one obtains a simple movement of the head in response to facial stimulation.

The alterations of fetal reflex responses during asphyxiation, indeed the fact of asphyxiation, were overlooked by Coghill and some of his followers. He studied *Amblystoma*, in which the nervous system is quite different from that of mammals at the time responses to stimulation of the surface can be elicited. Neural elements like those accounting for the amphibian "total response" are not present in mammalian embryos.

It is interesting to note that Coghill did not personally study mammalian embryos, with or without intact placental circulation. Herrick told me that he saw in Coghill's studies a basic concept of great significance, and he called Coghill's attention to it. He was impressed with the "Gestalt" idea. So Coghill searched the literature and found clinical reports of observations on human fetuses; he assembled these reports in a paper called "The Early Development of Behavior in Amblystoma and in Man" (2). I know of no better example of the fallacy of conceptualizing from data that are fragmentary and not fully understood. Coghill did not understand why experiments on mammalian fetuses removed to a dish of warm saline solution were any different from those on amphibian larvae in water. I know this, because he visited my laboratory and tried to convince me that I was in error in maintaining that it made a difference that a mammalian fetus was no longer attached to the endometrium. He simply did not understand this basic principle of mammalian physiology.

Why should we continue to allow the concept of "individuation from a total pattern" dominate our thinking? To be sure, there are gradients in development; the head end starts before the tail. But no mammal follows the exact pattern of *Amblystoma*, and we have no valid reason to hurdle the broad gap between the two species with this concept, philosophically attractive as it may be.

*Bodian:* Hooker agreed with Coghill.

*Windle:* Yes, Hooker agreed with Coghill, but he overlooked the reversals occurring during asphyxiation. Most work on the human has been with deteriorating fetuses. The only observations that I know of are the ones that Fitzgerald and I (9) made at the operating table; these were in a few early motile fetuses.

*Bridger:* Even in the newborn baby, the conditions determine the kind of reflex that can be elicited. If the oral zone is stimulated when the baby has just been fed, there is a withdrawal rather than a rooting response. Also, if the rooting response has been habituated and if the stimulus is applied with less than a 3-second interval, the baby, at times, turns the other way rather than rooting toward the stimulus. The response definitely appears to depend on the conditions at the time when the stimulus is applied.

*Sokolov:* May I discuss some results that were obtained in this experiment of Professor Luria's? I believe that the most important point about the physiological role of speech is that some functions are influenced by speech. For example, I think that change of blood pressure, change of attitudes to stimulation, change of reactivity of the brain can be influenced by speech and, as an example of this, I would like to tell you about some results which we have obtained in the activation of the orienting reflex during the elaboration of different motor reflexes. I have discussed with Dr. Lowell the activation of the orienting reflex through the verbal system, and I agree with him that the orienting reflex can be organized on the highest level, with the participation of speech.

For instance, in our experiment, when the instruction was given to count, the light stimulus (the same light which previously produced a very small effect in the occipital EEG) now evoked strong responses. This means that as a result of the verbal impulses, not only specific and voluntary controlled functions are influenced, but there is also some regulation of an activatory system or, as I believe, the reticular formation. This is also of importance for the understanding of two-way connections.

I think that the cortex, influencing in a very specific way the activatory system, is itself at the same time activated by these generalized responses through the reticular formation. This feedback is of very great importance for the understanding of the development of precise discrimination of stimuli in the elaboration of conditional reflexes. Such a mechanism shows that during the course of elaboration of conditional reflexes, some facilitatory mechanisms are at work. Such facilitatory mechanisms are not solely the function of the intensity of the applied stimulation, but are specifically connected with the meaning of the stimulation as well.

*Bodian:* This reminds me of something I was thinking about before, in relation to the discussion of speech; if speech is thought of as a complex sequence of movement, it can be compared with progression as a complex sequence of movement. Are there any associated movements in relation to speech, as there are in walking? Feedback is something that is inherent in the associated movements of walking, and perhaps in speech as well. The role of feedback can be both negative and positive; in a sequence of movements, a prior posture must be destroyed before a new one can be assumed. Is this the sort of thing you had in mind, Professor Sokolov?

*Sokolov:* I do not believe that functional speech can be reduced only to usage of symbols. The speech symbols are specifically related to the widespread responses produced in the brain. It is so that a word, a specific stimulus, can be very precisely differentiated from other words, but, at the same time, this stimulus can evoke a very strong generalized involuntary response.

*Fremont-Smith:* This ties in with one of the significant aspects of free association.

*Sokolov:* Yes, we have studied the orienting reflex to different word stimulations in man. We have presented different words to the subject, who was in a completely soundproof room. No responses were obtained to various familiar and usually applied words, but a very great vegetative response could follow some unusual word.

I would like to report an experiment that was conducted by Novikova in the laboratory of the Institute of Defectology. It concerned deafferentation in rabbits. Two different preparations were made, one with chronic acoustic deafferentation by transection of the acoustic nerves and the other with transection of the optic nerves. Quite different results were obtained. In the case in which optic nerves were transected, there was a very remarkable change. This consisted of a decrease of EEG activity and an increase of the threshold of movement evoked by direct electrical stimulation of the cortex. In other words, with the decrease in electrical activity of the visual and motor cortex following transection of the optic nerves, a drop in reactivity is observed. This indicates that the optical analyzer has a special role in the activation pattern.

This interpretation receives supportive evidence from the quite different patterns of electrical activity found in children and in adults with impaired hearing from those with impairment of the visual system. With impairment of the hearing system, the α-rhythm is increased, sometimes very markedly and in all leads. In cases in which the visual system is impaired, the α-rhythm of the occipital region is reduced and sometimes there is only the so-called Rolandic rhythm of the motor and precentral parts of the brain (29).

It is very remarkable that these people can be characterized by a decrease of their electrical activity in the occipital region. There are some criteria that are used in the clinic for testing visual discrimination in the blind and in the partially blind, and these were found to be in agreement with the degree of expression of the α-rhythm. Those children with a great amount of loss of visual acuity are characterized by a drop in electrical activity, and the children with a high ability of visual discrimination are characterized by preservation of the α-rhythm.

In this connection, quite an important theoretical problem arises. There are two general theories about activation of the α-rhythm: One is that a pacemaker exists between the cortex and the subcortical level. Possibly these experiments show that the α-rhythm arises in local points of the brain, and that stimulation from different analyzers via the reticular formation changes only the level of this local ability to produce these potentials and not the special pacemaker.

There is an interesting chapter in Wiener's latest book (37) on nonlinear problems of random theory. He devised a new theory of the α-rhythm. He made the assumption that a local potential existed, and devised a mathematical theory for the explanation of how, by postulating a separate oscillator, a dominance of one frequency can be preserved. His assumption was in good agreement with the experimental study of the power spectrum of the α-rhythm.

This is of importance for the understanding of the role of the reticular formation and the different analyzers in the study of rhythms. Perhaps these pacemakers are not so closely connected with subcortical functions. They may be more localized in the cortex, and the role of the subcortical levels may be only to change the conditions of these local oscillators. For example, these are only preliminary results, but we have calculated the coefficient of correlation between the reticular formation and the cortex. This is easy to do, but the coefficient of correlation characterizes only the linear relation between two magnitudes. Therefore, I cannot say whether or not some nonlinear relationship exists between oscillations of these two regions. But, in relation to the linear connection between the reticular formation and the occipital region, the coefficient of correlation was zero.

*Windle:* In considering deafferentation of the brain, it might be worth noting that the optic nerve brings more fibers into the brain than all other afferent nerves of the body combined, a million plus, in the human optic nerve.

*Doty:* This is in man, however, and in the cat—

*Windle:* I don't know the figure for the cat, but the monkey has 1,200,000 fibers and the dog has only 150,000. The fibers are all myelinated in these species.

*Doty:* Really? I know there are only about 118,000 fibers in the optic nerve of the cat and the dog (1).

*Pribram:* The same question can be asked about the relation between thalamus and cortex. What are the correlations between the *repetitive* activity of thalamus and cortex?

*Sokolov:* Unfortunately, we do not have these answers yet. This work is not finished, so I can report only preliminary results. By our method of calculation of the waves in the rabbit, there was no significant correlation between the reticular formation of the thalamic region and the motor region or occipital region, in spite of the coincidence between the frequencies.

*Lilly:* This remark is in regard to the deafferentation experiments in animals. As I have perhaps overemphasized in the past, if an adult human subject is isolated from stimuli to the extent that can be achieved by immersing him in water of the right temperature (94°F.) and keeping him in the dark, without sound or light, and if he is then freed from the gravity duties usually experienced outside of water, sleep does not ensue at all. Instead, there is an accumulation of energy and increasing restlessness with time. This is, in fact, the fastest way I know of to get a very rapid rest without sleep.

These experiments were done because of the deafferentation story and because of Dr. Magoun's work and that of others interested in this kind of picture. We wanted to have as normal a preparation as we could, that is, physiologically normal in the sense of having the nervous system intact including all the peripheral feedbacks, and then to eliminate as much as possible the portions of the feedback loops that went out into the external reality beyond the skin.

If animal preparations in deafferentation experiments are re-examined from the standpoint that there may be something else involved here, such as damage or interference with various kinds of excitatory circuits and inhibitory circuits, I think the problem is sharpened by the knowledge that if the organism is intact but freed as much as possible from stimulation, there is an accumulation of energy rather than a sleep state.

I just wanted to get that in because it seemed to me, at least in terms of the animal experiments, to sharpen them up a bit.

These results we obtained in 1953, 1954, and 1955. Confirmatory findings were made in England by A. M. H. Bennett at Farnborough R.A.F. and at Portsmouth, in the Royal Navy. Bennett had six subjects in whom he had a successful run, without panic and without any adverse effects on the subject. He had three subjects who became panic-stricken or in some way were disqualified for the experience.

If there is any pain left, any residual discomfort under these circumstances, due to acute angulation of the neck or too much mask pressure or a bad seal on a mask or something like that, the subject is quickly worn out. This is a very wearing and fatiguing experience if pain is present. I bring that out because, in some of these animals, I suspect that there may be, and there probably is, intense pain, which could wear the preparation out very rapidly and lead to sleep; so I still think there is a lot left to be done on all of these preparations.

When stimulated with implanted electrodes in some of these areas, especially in the mesencephalic region, the unanesthetized animal shows intense pain. There are very powerful, painful experiences in that area, and there are also extremely rewarding experiences that can be brought about in the area. In other words, it is a very potent region for very powerful influences which can quickly wear an animal down. I just want to bring these up as possibly complicating factors to interpretation of some of these results.

*Purpura:* I am not surprised that correlations are rarely observed in the studies mentioned by Professor Sokolov. A 5-per-sec. pattern of activity in EEG tracings from a particular region of somatic sensory cortex need not be associated with a similar pattern of activity in the thalamic relay nucleus with specific projections to that area of somatic sensory cortex. Such EEG "discharges" are rarely correlated with conductile activity in thalamocortical or corticothalamic pathways.

*Livingston:* Dr. William F. Caveness* in New York has learned something important about the spread of excitation down the neuraxis in relation to development. He has examined the capacity of the infant monkey, as compared with the adult monkey, to exhibit an extension or "spread" of seizure discharges, descending from the motor cortex down to the motor horn cells. There is a spectacular difference according to age. By inducing spiking at the cortical level, using penicillin, he has shown that spikes appear locally just as soon in the 2-day-old or 10-day-old monkey as they do in the adult monkey, but they do not reach the motor outflow nearly as soon. In the infant monkey, within a few days of birth, about 1½ hours are necessary for the seizure discharge to "spread" to the point where it involves the arm and leg on the contralateral side. The seizure discharge rarely spreads to involve the limbs on the ipsilateral side. In the adult monkey, however, the same treatment can "spread" to involve both sides of the body, and this becomes fully developed within 7 minutes following the local cortical injection of the penicillin.

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*Personal communication.

Between the infant monkey and the adult, *i.e.*, in animals at 6 months of age, Dr. Caveness finds that it takes about 45 minutes for the seizures to "spread" to the motor outflow of the contralateral arm and leg.

*Doty:* I would like to present some ideas that might bring our thinking back more specifically to the central nervous system. It is rather fitting that they be presented at this conference, since these thoughts first began to develop 10 to 12 years ago, when I was a student of Dr. Hess's.

Many of the highly complex behaviors which we have been discussing, such as the fascinating contributions from the ethological school or much of conditional reflex physiology, including acquired human behavior of a stereotyped nature, can in their essence be described as intricately organized, specific outputs of the nervous system in response to highly specific inputs. Since input exists effectively only as a pattern of neural activity, it is obvious that an "input" for a given behavior can be generated by activities entirely within the brain without immediate recourse to external causes.

There are available in the central nervous system many neural organizations which can be analyzed in these terms, in which it should be possible to define the input-output relationships, the nature of the effectiveness of one versus another efferent pattern, and the manner of efferent integration and control. One of the most convenient and instructive of these neural organizations is that controlling swallowing —a very prosaic but exceedingly complex act.

Figure 192 charts as much as we know of the organization of this system. The term *swallowing center* is not an anatomical designation. It refers to those neurons, probably widely scattered in the medulla, which are functionally interlocked and the excitation of which commands the motor nuclei in the specific spatio-temporal sequence of their activity in swallowing. This action endures for some 500 msec. in the pharyngeal region and proceeds down the esophagus for several seconds—times hard to understand in terms of synaptic delays. In 1888, Wassilieff (35) showed that a medullary section excluding the action

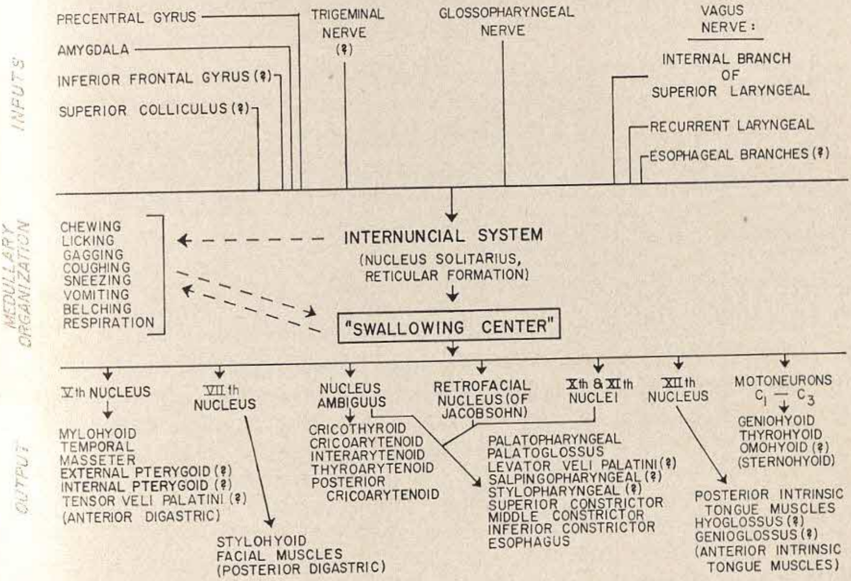

FIGURE 192. Summary of the neural organization of deglutition. Further experimental confirmation or analysis would be desirable regarding participation of those elements followed by question marks. Muscles designated in parentheses showed little or no activity during deglutition in the anesthetized animal. In man the masseter, temporal, and facial muscles seem to be active in most swallowing (5).

of the mylohyoid muscle, which leads the firing sequence, did not patently disturb the remainder of the sequence. Thus, one would infer that the "swallowing center" is not merely a linkage between pools of motoneurons, and certain EMG evidence (5) is concordant with this view. The synergy also proceeds independently of proprioceptive feedback (5) and (28) much as the egg-rolling of the gray goose proceeds independently of the egg (23), the preening reactions in the absence of tail feathers (22), or the imprinting of song characteristics before a bird can sing (33).

The general coordination of excitation and inhibition of motor nuclei during deglutition is remarkably constant, though the behavior of individual motor units seems unpredictable. Figure 193 is an example of this constancy under various background states of the central nervous system. Thus, from the "statistical" behavior of the motor units, a highly stable efferent pattern is somehow achieved.

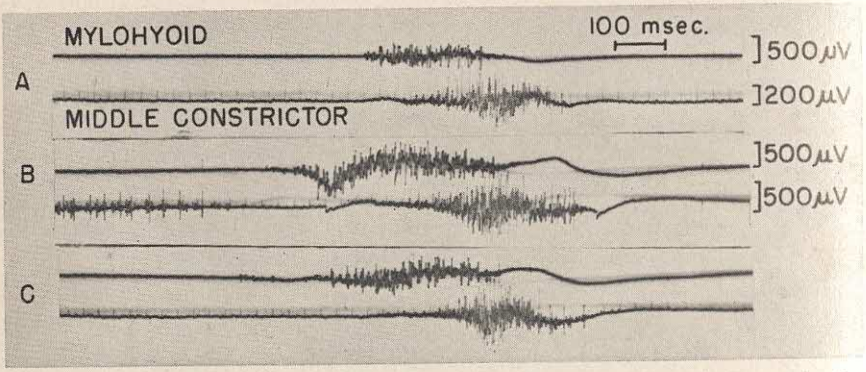

FIGURE 193. EMG's during swallowing under different conditions of anesthesia: (*A*) deep ether; (*B*) 2 hours later, cervical cord cut, local anesthesia; and (*C*) 5 minutes after 10 per cent anesthetic dose of nembutal. Note consistency in phasing of excitation in the two muscles despite variation in over-all duration and discharge pattern of motor units. Reprinted, by permission, from Doty, R. W., and Bosma, J. F.: An electromyographic analysis of reflex deglutition. *J. Neurophysiol.* **19**, *44-60 (1956)*.

This efferent pattern is also independent of type or source of afferent input. However, the afferent portal of the controlling center is highly selective (4). In this pluripotential region of the pharynx, it is probable that one pattern of input leads to swallowing, another to gagging, another to coughing, etc. With electrical pulses applied to the superior laryngeal nerve, respiratory effects are obtained with any stimulus frequency, but swallowing does not occur at moderate stimulus intensities if the frequency is too high (*e.g.*, 100 per sec. in the dog). I have called this the limiting frequency. It is probably related to summation of subnormality (21) and has been observed in single spinal interneurons (11). There is also an optimal stimulus frequency which is species-characteristic and at which swallowing occurs with shortest latency, lowest threshold, and most rapid continuing rate. The basis of this feature of the swallowing center's input selection is more difficult to understand than is the limiting frequency phenomenon. Figure 194 shows that optimal responsivity is maintained by stimulus patterns differing widely from the optimal monotonic frequency. Such analysis shows: (a) optimal responsivity does not result from phasing of incoming stimuli with excitatory cycles of the "center"; (b) each synchronous afferent volley contributes to an excitatory state in equal degree almost without regard to its position in a pulse series, *i.e.*, the central mechanism appears to "count" each pulse delivered from 5 to several hundred msec. after each other; and (c) the excitatory state, although it endures for sec-

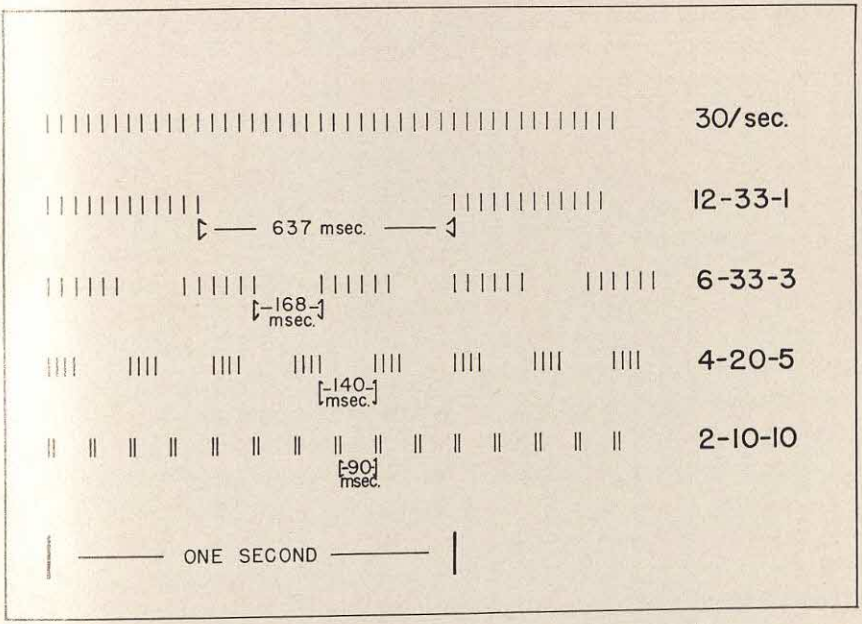

FIGURE 194. Scale drawing of temporal relations of stimulus pulse patterns applied to superior laryngeal nerve of dogs. All these patterns were able to evoke deglutition optimally. The numbers indicate: number of pulses, milliseconds between pulses within group, repetition rate of group, *e.g.*, 4-20-5 signifies a group of four pulses, 20 msec. between each pulse with the group of pulses repeated five times per second (hence totaling 20 pulses per second). Reprinted, by permission, from Doty, R. W.: Influence of stimulus pattern on reflex deglutition. *Am. J. Physiol.* 166, *142-158 (1951).*

onds, declines after each volley, so that repeated volleys must summate to attain threshold. Yet one volley following too rapidly (within 5 msec.) after another encounters refractoriness which increments with each volley at some station prior to that summating the excitatory state. Hence, the stimulus input is integrated by these summating and decaying processes of refractoriness and excitation. In the natural situation, the spatial as well as temporal aspects no doubt contribute an additional complexity which must also be integrated by the center; this, then, "accepts" only certain spatio-temporal combinations and "rejects" others (which in turn may be adequate afferent organizations of other centers).

It is encouraging that, though the experimental opportunities have barely been opened, it is already possible to speak of this behavior in terms of neural operations, and to define certain definite possibilities and exclude others. And can we not go further? Applying one's foot to the brake upon seeing a red light and a skilled musician's motor output as he sight-reads a cadenza are learned performances, and they appear in an operational definition to be of the same genre as swallowing: accurate and reproducible outputs triggered by highly specific inputs. Time precludes discussion of the problem of background setting of the system by its preceding activity, by other inputs, by hormones, by past events, etc., which can obviously be of great importance. Yet I think one can see in the afferent and efferent specificities of "simpler" systems, such as that of deglutition, a paradigm for these learned reactions, for the "neural models" Dr. Sokolov postulates, or for responses which W. R. Hess (14) was able to trigger by diencephalic stimulation. Some of the behaviors which Hess induced can be thought of in terms of hierarchies of centers. Thus the stimulation which produces bulimia or activates a *Fresstreib* perhaps excites a center which in its turn controls and integrates the centers of salivation, licking, mastication, swallowing, and limb and head movements associated with feeding. Stereotyped behaviors that are of significance to the ethologist may also be evoked by electrical excitation. Grimm (13) has elicited integrated feeding behavior in goldfish by electrical stimulation of the olfactory systems, and I understand from Dr. Fremont-Smith that von Holst* has produced, by stimulation of the hypothalamus, typical brooding and flight reactions in chickens.

Graham Brown (12) long ago reported a "goal-seeking" behavior from stimulation of the superior frontal convolution in monkeys. This produced turning of the head with eyes fixed with relation to the head; but if the head were held, the eyes moved to achieve the same endpoint of fixation. Hyde (17) has now demonstrated rather similar "centers" at brain stem levels. These two experiments considered together suggest that the movements seen on cortical stimulation arise through cortical command of subcortical centers which coordinate the movement. In other words, the "motor" cortex may not be much concerned with organization of movement but rather selects which subcortical hierarchies are activated (and, of course, there are spinal hierarchies such as the scratch reflex and running patterns).

Figure 195 illustrates what I believe may be such a cortical activation of a subcortically organized synergy. For the primate on the right, I cannot specify the stimulus, though the motor output of arm flexion and mouth opening is patently similar to that of the primate on the left, even to retraction of the tongue. The movement on the left was

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*Personal communication between Dr. Frank Fremont-Smith and Dr. Erich von Holst.

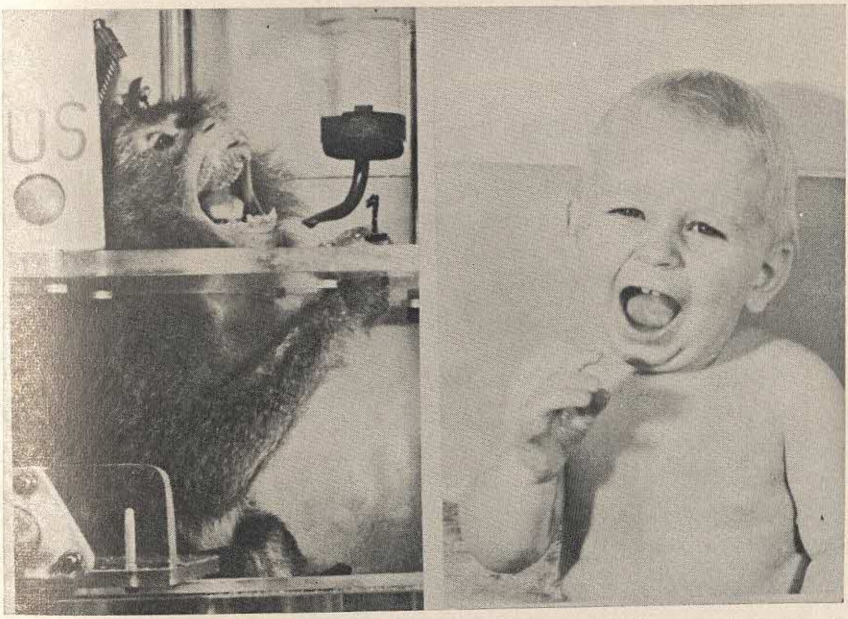

FIGURE 195. Similar synergies in different primates which were fortuitously captured on the same roll of film.

elicited by 50 1-msec., 0.2 mA. pulses applied to left precentral gyrus within 1 second. A nearly identical end-point of motor coordination was found by Delgado for stimulation at the rhinal fissure (Figure 1 in ref. 3).

Such coordinations of mouth opening with arm flexion are a prominent feature of primate feeding patterns, appearing ontogenetically at the "everything in the mouth" stage of the child in Figure 195. One might argue that for the monkey in Figure 195 the electrodes overlapped "hand" and "mouth" areas of "motor" cortex, producing concurrent activity. If so, does rhinal fissure stimulation then also activate this same cortical region? I think it rather more likely that both rhinal cortex and motor cortex are playing into a "hand up—mouth open" center existing at lower levels. First, were the electrodes actually in the coordinating center, the electrical stimulation would probably disrupt the coordination. Second, electrodes at widely scattered cortical and subcortical loci may evoke a particular movement in a particular animal; *i.e.,* the same movement can be obtained by stimulation from different loci (6). Further, stimulation at any cortical (and certainly many subcortical) points can, through training, be made to elicit a selected movement and the same movement is then readily elicited by stimulation at other cortical points with much less training (7).

Stimulation of the "visual" cortex of the monkey in Figure 195, when it was consistently accompanied by stimulation of "motor" cortex eliciting the movement shown, altered the systems so that stimulation of "visual" cortex produced flexion of the arm (6) with a threshold of 0.55 mA. Then, an uncomfortable shock applied to the animal's tail was substituted for the "motor" cortex stimulation. An extensor movement was required to terminate this discomfort, or to avoid it if made to "visual" cortex stimulation. There was a period of confusion in which "visual" cortex stimulation produced strong flexion responses followed by extension; but ultimately a pure extensor response was obtained at a threshold of 0.2 mA. Thus, the same stimulation of the same cortical point can mediate different coordinations depending upon the past history of the animal. "Visual" cortex is not known to have inherent connections of any consequence to cervical cord, or to have the capacity to reorganize them from flexor to extensor motoneurons. These results thus suggest that some intermediate system operates as a neural center, which, under the influence of stimulus pairing, alters its threshold or afferent organization to the point where the excitation complex emanating from "visual" cortex can trigger it. The lowering of the threshold is best maintained by a loosely defined system we call "motivational," and in such a circumstance the center becomes more accessible to the "visual" cortex input and to other inputs given in the presence of this motivational background.

Finally, the stimulation of the "motor" cortex itself, which inherently produces the movement shown in Figure 195, can be made to elicit the same extensor movement as that produced by the "visual" cortex stimulation; and the threshold for the conditioned, extensor movement is lower than for the inherent movement. Of additional interest is the fact that stimulations of precentral gyrus at intensities which produce no apparent movement nonetheless have a great subliminal effect and seem to prepare the motor system to execute the same movement which higher intensities evoke. This "set" of the system is revealed during subliminal cortical stimulation if the animal's tail is shocked or a loud, unexpected auditory stimulus presented. At such times, the motor system is thrown into violent activity exactly as though the stimulating current at the cortex has been increased several fold. The effect is particularly dramatic in monkeys attempting to make extensor movements of the arm to terminate the tail shock, but unable to do so because this arm has been captured in flexion by the summation of cortical and tail stimulation. The conditioned extensor movement can be made if the cortical stimulus activates the nonconditioned arm. The summation of cortical and tail shock stimuli may be so overpowering as to produce convulsive afterdischarges. The site of this summation is, of course, unknown; but I will be very surprised if it turns out that both auditory and tail afferent excitation appear at whatever site on precentral gyrus we choose to place our subliminal stimulus!

## REFERENCES

1. BRUESCH, S. R., and AREY, L. B.: The number of myelinated and unmyelinated fibers in the optic nerve of vertebrates. *J. Comp. Neurol.* 77, *631-665 (1942).*
2. COGHILL, G. E.: The early development of behavior in Amblystoma and in man. *Arch. Neurol. & Psychiat.* 21, *989-1009 (1929).*
3. DELGADO, J. M. R.: Prolonged stimulation of brain in awake monkeys. *J. Neurophysiol.* 22, *458-475 (1959).*
4. DOTY, R. W.: Influence of stimulus pattern on reflex deglutition. *Am. J. Physiol.* 166, *142-158 (1951).*
5. DOTY, R. W., and BOSMA, J. F.: An electromyographic analysis of reflex deglutition. *J. Neurophysiol.* 19, *44-60 (1956).*
6. DOTY, R. W., and GIURGEA, C.: Conditioned reflexes established by coupling electrical excitation of two cortical areas. *Brain Mechanisms and Learning.* J. F. Delafresnaye, Ed. C.I.O.M.S. Symp. (In press).
7. DOTY, R. W., and RUTLEDGE, L. T.: "Generalization" between cortically and peripherally applied stimuli eliciting conditioned reflexes. *J. Neurophysiol.* 22, *428-435 (1959).*
8. ERIKSON, E. H.: The roots of virtue. *The Humanist Frame.* Sir Julian Huxley, Ed. New York, Harper (In press).
9. FITZGERALD, J. E., and WINDLE, W. F.: Some observations on early human fetal movements. *J. Comp. Neurol.* 76, *159-167 (1942).*
10. FRADKINA, F. J.: The genesis of speech in children. *Proc. Hertzen Pedagog. Inst., Leningrad* 112 *(1955).* (In Russian).
11. FRANK, K., and FUORTES, M. G. F.: Unitary activity of spinal interneurones of cats. *J. Physiol.* 131, *424-435 (1956).*
12. GRAHAM BROWN, T.: Reflex orientation of the optical axes and the influence upon it of the cerebral cortex. *Arch. néerl. de physiol.* 7, *571-578 (1922).*
13. GRIMM, R. J.: Feeding behavior and electrical stimulation of the brain of *Carassius auratus. Science* 131, *162-163 (1960).*
14. HESS, W. R.: *Das Zwischenhirn.* 2nd Edition. Basel, Benno Schwabe, 1954 (p. 81).
15. HOMSKAYA, E. D.: Investigation of the influence of verbal reactions on motor reactions in children with the cerebro-asthenic

syndrome. *Problems of the Higher Nervous Activity of Normal and Abnormal Children.* Vol. II. A. R. Luria, Ed. Moscow, Academy of Pedagogical Sciences Press, 1958. (In Russian).

16. HOOKER, D.: Fetal reflexes and instinctual processes. *Psychosom. Med.* 4 *(No. 2), 199-205 (1942).*
17. HYDE, J. E., and EASON, R. G.: Characteristics of ocular movements evoked by stimulation of brainstem of cat. *J. Neurophysiol.* 22, *666-678 (1959).*
18. KOLTZOVA, M. M.: *The Formation of Higher Nervous Activity in Children.* Moscow-Leningrad, Medical Press Publishing House, 1958. (In Russian).
19. LANGWORTHY, O. R.: Correlated physiological and morphological studies of the development of the electrically responsive areas in the cerebral cortex of the opossum. *Contrib. Embryol.* (Carnegie Inst.) 19 *(No. 103), 149-176 (1927).*
20. ———: Histological development of cerebral motor areas in young kittens correlated with their physiological reaction to electrical stimulation. *Contrib. Embryol.* (Carnegie Inst.) 19 *(No. 104), 177-208 (1927).*
21. LORENTE DE NÓ, R., and GRAHAM, H. T.: Recovery cycle of motoneurons. *Am. J. Physiol.* 123, *388-399 (1938).*
22. LORENZ, K.: Morphology and behavior patterns in closely allied species. *Group Processes.* B. Schaffner, Ed. Trans. First Conf. New York, Josiah Macy, Jr. Foundation, 1955 (p. 171).
23. LORENZ, K., and TINBERGEN, N.: Taxis und Instinkthandlung in der Eirollbewegung der Graugans. *Ztschr. Tierpsychol.* 2, *1-29 (1938).*
24. LUBLINSKAYA, A. A.: *Essays on the Mental Development of the Child.* Moscow, Academy of Pedagogical Sciences Press, 1959. (In Russian).
25. LURIA, A. R.: *Essays on the Psychophysiology of Writing.* Moscow, Academy of Pedagogical Sciences Press, 1950. (In Russian).
26. ———: *Traumatic Aphasia.* Moscow, Academy of Medical Sciences Press, 1947. (English Translation - Hague, Mouton Press, In press).
27. ———: *Rehabilitation of Brain Function after War Trauma.* Moscow, Academy of Medical Sciences Press, 1948. (English Translation - London, Pergamon Press, In press).
28. MUHLBERG, W.: Swallowing in curarized animals. (Cited by H. Kronecker in Deglutition) In: *Dictionnaire de Physiologie.* Vol. IV. C. Richet, Ed. Paris, 1900 (p. 754).
29. NOVIKOVA, L. A., and ZEMTSOVA: The study of the functional state of the brain in blind subjects by means of the EEG method. *The Scientific Conference on Defectology Problems.* Moscow, 1955. (In Russian).
30. PAVLOV, I. P.: Essay on the physiological understanding of hysteria - Conditional reflex. In: *Twenty Years of Objective Analysis of Higher Nervous Activity. Complete Works.* Vol. III. 1949 (pp. 476, 568-569).

31. Sokolov, A. N.: Investigation on the problem of speech mechanisms of thinking. *Psychol. Sciences in USSR.* Moscow, Academy of Pedagogical Sciences Press, 1959 (pp. 488-515). (In Russian).
32. Spirin, B. G.: Disturbances in plasticity of the nervous processes after operations on the human brain. *Dissertations - Academy of Medical Sciences.* Moscow, 1951. (In Russian).
33. Thorpe, W. H.: The process of song-learning in the chaffinch as studied by means of the sound spectrograph. *Nature* 173, *465-469 (1954).*
34. Vygotsky, L. S.: *Selected Psychological Papers.* Moscow, Academy of Pedagogical Sciences Press, 1956. (In Russian).
35. Wassilieff, N.: Wo wird der Schluckreflex ausgelöst? *Ztschr. f. Biol.* 24, *29-46 (1888).*
36. Werner, H., and Kaplan, E.: The Acquisition of Meanings. *Monographs Soc. Res. in Child Development.* Vol. XV (No. 1). 1950.
37. Wiener, N.: *Nonlinear Problems in Random Theory.* New York, John Wiley & Sons, 1959.
38. Windle, W. F., Becker, R. F., Rhines, R., and Cowgill, E. J.: Effect of anoxia on trigeminal reflexes in cat fetuses. *Physiol. Zool.* 15, *375-382 (1942).*
39. Zeigarnik, B.: *Disturbances of Thinking in Mental Illness.* Moscow Univ. Press (In press). (In Russian).

# SIGNALING SYSTEMS IN THE DEVELOPMENT OF COGNITIVE FUNCTIONS

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MY WORK HAS BEEN with neonates, 3-day-old babies, and I have already presented some of these data in the discussion of Professor Sokolov's paper. This work is concerned with the possibility of using measurements of autonomic responses both to differentiate one baby from the other and to see the influence of organismic or temperamental factors in future personality development. The data are in agreement with some of the evidence which Professor Sokolov has presented with respect to habituation and sensory discrimination. However, since I have always been interested in Pavlov's (35) concepts of signaling systems, I have tried to relate these Pavlovian concepts to ideas that have been used in this country and in others with respect to the development of cognitive functions.

Since antiquity, two of the most fundamental questions facing philosophers are: What is the world, and how do we know it? This paper attempts to deal with the latter question—how do we get to know the world? After much thinking about Pavlovian concepts, I feel that perhaps signaling systems would be one way of integrating the three main levels involved in the problem of cognition—that is, neurophysiology, psychology, and society. It is true that this is an ambitious project, but let us survey the field and attempt to speculate with this orientation.

First, I shall give a description of Pavlov's theory of signaling systems: He felt that, in common with other animals, man has unconditioned or inborn reflexes and instincts, as well as primary conditioned responses, formed from a first signaling system, such as sensations, perceptions, and direct impressions of their environment. In addition, he believed that man has a second system of signals of reality which includes speech, ideas, or verbal thoughts, abstractions, and generalizations. Pavlov stated that the direct impressions of objects and phenomena of the external world are the first signals of reality and that the verbal symbols or verbal designations of these impressions are the second signals of reality. Every word is related to some direct object or function or action in reality.

The Soviet philosopher, Georgiyev (13), a colleague of Professor Luria's, has tried to integrate these two signaling systems into a general theory of cognition. He states that man is endowed with two qualitatively different forms of cognition: the sensory or perceptual and the rational. He states that personal direct practice or experience is the basis of the formation and origin of perceptual cognition, while speech or the symbolic function is the basis of so-called rational intelligence.

Within the bounds of Pavlov's first signaling system, with its physiological mechanism common to both animals and man, Georgiyev places all forms of this sensory or perceptual cognition, that is, sensation, perception, and representation of sensory images. The rational form of cognition or thinking is based on what he called the second signaling system, the symbolic function that enables man to make abstractions and generalizations, and thus to form concepts and draw logical conclusions.

This rational form of cognition gives man the ability to rearrange and reconstruct the data of his perceptions, so that he grasps reality, not only according to the appearance of things, but also in terms of lawful relationships and interactions between things. This second signaling system can achieve this because it can use knowledge of things indirectly experienced or communicated. It is not wholly dependent on personal experience. This tendency to divide human cognition into two systems, the first and second signaling systems, the sensory or perceptual and the rational, is evident in the writings of workers from various frames of reference.

Freud (9) divided human thinking into two basic systems, the conscious and the unconscious—the unconscious being guided by what he called primary process laws and the conscious by secondary process laws. As presented by Freud, in primary process thinking, which is present in dreams and schizophrenic thinking and at times in free associations, an idea is that of a thing alone—the direct memory image of the thing, and the associations of things are based on emotional or direct personal experiential linking of things, unhampered by rational concepts. In secondary process thinking, the conscious idea comprises the concrete idea of the thing, plus the verbal idea corresponding to it. This verbal idea arises from consensual validation and the need for communication, and the laws of association are, for the most part, logical and based on this need for social communication. I would imagine that Pavlov's concepts of first and second signaling systems are at least analogous to these phenomena.

Sullivan (43) also divides human cognition into two basic processes. The first is the prototaxic and parataxic modes, which refer to direct concrete sensations and experiences which are not related to each other in a logical way but, rather, linked only by what he called the natural way of such occurrences, similar to Pavlov's first signaling system and inborn reflexes. The syntaxic mode, which is Sullivan's term and seems to be similar to Pavlov's second signaling system, includes consensually validated speech and symbolic activity acquired from interpersonal experiences and governed by logical principles, accepted as true but not necessarily directly experienced.

Piaget (36) divides human thought fundamentally into (a) sensori-motor intelligence, again similar to Pavlov's first signaling system and unconditioned reflexes, and into (b) what he called conceptual intelligence. Sensori-motor intelligence, according to Piaget, coordinates successive perceptions and actions which are real entities and links them temporally and causally but does not explain or classify them. It is based on and is part of action or practice, and is in no way reflective. It never concerns anything but real objects and responses actually carried out.

Conceptual intelligence and formal thought develop from sensori-motor intelligence and follow many of its laws of acting, but its main function is the use of symbols, not in an egocentric manner, as Piaget called it, but as a means of social communication and classification according to logical laws.

In studying the origin of this intelligence in children, Piaget described the use of words and ideas in the so-called concrete or, as Professor Luria would call it, impulsive manner. That is, in the process of development of the second signaling system, words and verbal images are handled initially as signals of the first signaling system. I think Professor Luria gave good evidence for that.

From another frame of reference comes Goldstein's (14) division of thinking into two areas, the abstract or rational attitude, and a concrete and emotional language or, as he called it, behavior, since it is learned from direct experience. Goldstein feels that a percept of emotional experience belongs to a different level of organization from abstract speech, even though the same verbal symbol may be present at both levels. Thus, words at different times and in different conditions may be signals belonging to the first or second signaling system or, more often, to both simultaneously, as in the Pavlovian conception of the use of language.

In trying to understand human cognition, I think it is important first to determine what are the laws of the functioning of the first signaling system, and then to see what are the mechanisms of the development from the first to the second signaling systems.

According to Pavlov, both signaling systems are governed by what he called the general law of temporary nervous connections and associations. However, the first signaling system deals only with signals or signs which are part of the physical world. An object becomes a signal only through direct individual experience or activity. Signals and signs are the hallmark of the animal world, and the so-called conditioning learning theories are directly relevant to this level of adaptation.

Werner (45) described a syncretic, indivisible, diffuse unity between the animal and the environment. According to him, the perceptions of the animal exist only in so far as they are part of a wider totality of the animal's actions. Things do not stand out there, discrete and fixed in meaning with respect to the cognitive subject. They are intrinsically formed by the psychophysical organization of which they constitute an integral part, by the whole vital motor affective situation. Hence, he speaks of "things of action" or of "signal-things" in such a primitive world.

The animal knows the object only in terms of its immediate reaction to it. Animals, in contrast to man, cannot learn more than they have practiced. Applying principles from both contiguity and reinforcement learning theories, perhaps we can understand the workings of the first signal system or animal and biological intelligence.

*Harlow:* As a zoologist, I object to the term, "the animals," just as we don't say, "the monkey." There are many animals. There are all kinds of ranges and capabilities. I think the assumption that no animal is capable of what we would call abstract thought is nonsense.

*Hess:* I agree.

*Harlow:* As a matter of fact, Goldstein inspired me because, during a series of lectures, he implied that no subhuman animal could do this kind of thing.

*Bridger:* It all depends on defining "abstract."

*Harlow:* Animals, particularly the primates and some of the other carnivores, really do have abstract concepts. They don't possess the tremendous number that man does, nor are their concepts as wide-ranging, and they certainly don't have the capability of communicating these concepts to each other.

*Pribram:* I'm not so sure of that.

*Bridger:* They can only learn by direct activity.

*Pribram:* They can learn from watching.

*Bridger:* That is only imitation. I say they can learn only through direct experience with the other animal or environment, and not through mediated communicated experience.

*Luria:* I think this is a very important matter. The animal has two kinds of development, the first is the instinctive or unconditioned experience of the species, and the second is a conditional reflex—the experience of the individual. Man, who has the second signaling system, has a third potential, which is to learn, to accumulate the experience of whole generations, via speech. This is specific to man and means that he has a third form of development which is not available to animals. Man can transmit the experience of generations, of thousands of years, as well as new modes of behavior by using his language. No dog can transmit the experience of generations.

Therefore, I would propose a different sequence from the one proposed by Dr. Bridger, who put the first stage at the physiological level, the second at the psychological level, and the third, at the sociological level. The first is physiological, the second is the sociological level, and the third is the psychological level. Why? Because psychological processes in man are the result of the combination, the coincidence, the synthesis of biological and social experience, and what we are dealing with when we talk about mental processes are processes which have been acquired by means of speech, by verbal ability, or by appropriation of a social experience. That doesn't solve the problem, but for me the sequence of levels is different.

*Pribram:* At Stanford, we have been teaching the medical students their first introduction to clinical medicine. We organize the course around the same point Professor Luria has just made; we do *not* talk about the physiological level, then the psychological, and then superimpose on this the social as a third level. Rather, we talk about the social and the physiological factors and their convergence to produce behavior. Our convergence of thought is really remarkable.

*Hess:* I would like to speak about the problem of the acquisition of signaling systems in animals. Research on this has been going on for some time by Frings (10), who has been working with communication in crows. Crows have a rather complex signaling system. We might almost talk about it as a kind of language. He has found that a crow from one part of the country may not necessarily understand the signaling system of a crow from another part of the country, which would certainly, I think, lead us to the suspicion that this signal system set is transmitted by some kind of social interaction. I suspect, that at least one such instance will be found in which an animal is capable of a particular ability, and we will again have to modify these big generalizations about man.

*Fremont-Smith:* Lorenz* cites an example of a carnivorous fly, which kills other flies. The male, wishing to mate with the female, is in some danger of being eaten by the female which is larger than he is. However, he often catches a smaller fly, which he wraps up in silk and presents to the female. While she is busy taking it apart and eating it, he proceeds to mate with her. In some instances, however, the male does not have to catch a fly at all. He merely wraps up some silk and hands it to the female, and this succeeds in its purpose. It seems to me that this is also very close to the symbolic level.

I agree with the viewpoint that there isn't any such sharp breakdown between the human and the subhuman, that this is a transition. This is a process of transition in the evolutionary sense, and I think it is only because of our preconceptions that we make quite such a sharp division; that there is a major difference, there is no question, but it is a transition point in a spectrum rather than a sharp division.

*Luria:* There are some important specific differences between the so-called languages in animals and the essentials of the language of man, his historic social language. Many forms of so-called languages in animals have been studied; for example, in our country there has been some fine work on the so-called language of bees.

But in all this so-called language there is something lacking. In German, this is called *Darstellungfunktion*; that is, a language as a basis for the second signaling system has one principal feature, the symbol. The symbol replaces the object, not the emotional situations. The so-called languages of animals lack this object symbolization. Their sounds are always expressive signals, and not nominative signals, and of course not categorical signals.†

*Hinde:* Professor Luria has said very much what I wanted to say, and I couldn't agree more fully with him. There is a great danger, in these instances of crows and flies which we can describe in the same sort of words as we use to describe human behavior, of reading more into them than is really there. The point is very well made by Koehler's (22) experiments on counting in animals, birds, and lower mammals, in which he shows that they can count up to 5, 6, or 7, which is as far as we can count without naming numbers. This illustrates both the extraordinary and surprising complexity of the things these animals can do and, at the same time, how they lack this verbal ability which would enable them to go further.

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*Personal communication.

†EDITOR'S NOTE: A differentiation of brain mechanisms for communication by means of emotional vocalization as contrasted with those for symbolic language is to be found on pages 43 and 44 and Figures 61 and 62 in the section on the Evolution of Man's Brain, contributed to this volume by H. W. Magoun, L. Darling, and J. Prost.

*Hess:* I want to give one example that is extremely clear and which would refer to Professor Luria's point; that is, the chicken has a warning call to describe the fact that an aerial predator is coming. This is quite different from the warning call which describes the fact that a ground predator is coming. I think this would fit the definition that you are talking about. It is difficult for me to conceive of an emotional response which does not take into account a different kind of object.

*Luria:* It designates objects only in a certain situation and does not designate objects outside of this situation.

*Lilly:* I also have spent a little time in thinking about some of these problems but in a different context. When dealing with animals with larger brains, I find that I am hard pressed in making comparisons with the smaller-brained animals.

In a situation in which I had a bottle-nosed dolphin living with two other dolphins, I kept one of them out of the tank for too long a time in cold water at 53°F. This was too cold for him and as a result he developed an S-shaped curve in his spine and couldn't swim. When we put him back in the tank with the two others, he immediately sank to the bottom and gave the distress call (which we had already identified by other means). The two other dolphins came over and lifted him to the surface. Then we heard a lot of whistling and twittering sounds, and the dolphins immediately changed their tactics. Instead of swimming under his head and lifting him to the top so that he could breathe, the way they did on the distress call the first time, the second time, they came and raked him across the ano-genital region with their dorsal fins, causing a reflex contraction of the flukes which then propelled him to the surface.

In another situation, we had kept another dolphin under anesthesia and had damaged his brain. He kept falling over to the right when he was trying to swim. He gave the distress call when we put him back in the tank and the other dolphins came under his head and lifted him to the surface so that he could breathe. Then, a lot of twittering occurred.

Apparently there was a verbal exchange going on. I say "apparently." They then changed their tactics and began to swim beside him, on the side toward which he would fall, so he had something to press against, which would then hold him up.

I thus illustrate a sequence. No. 1, an animal in personal distress emits a signal, which is a very stereotyped call and which is characteristic for all animals, including man; that is, each species has its own distress call. That is an obvious emotional expression of the type that has been discussed here. No. 2, the other animals make a social response in that they come over and immediately do that thing which is in response to that call, the emotional response of lifting him to the surface and getting him to the air; in other words, it is a first-aid kind of answer. Then, a subsequent series of sounds exchanged between all the animals involved, with a solution to the distressful situation that is appropriate to that situation, and not necessarily the first solution that was proposed. It is an elaborated solution, appropriate to the kind of lesion or problem that the animal has.

These are much better differentiated things; so the language is denotative, nominative, predictive, and descriptive, as it were. It has all these properties, and I think there are probably other properties of such a language, which the smaller-brained animals cannot have; in other words, the length of the sequences involved, the complexity of the situation, the number of variables that are taken into account, and all the rest of this is what is important.

*Pribram:* There aren't really good ways of describing what we are trying to say here. Our language isn't adequate as yet. However, an example can be given of a child: A child will say, "A hole is to dig." But this is different from what Professor Luria is saying when he states that, in essence, the set of alternatives and the units for measuring them are specified in our language. Animals other than man may indicate that "a hole is to dig," but they can't make an alphabet, which is manipulable: in an alphabet the letters can be interchanged and maneuvered around according to a structure or plan. It is this characteristic which defines human language. I think this is what we are trying to say, that language is programmed.

*Bodian:* Man is a grammatical animal.

*Pribram:* That's part of it, but not the whole story. At the Behavioral Science Center, we searched for some answers to this question last year. Our tentative conclusion was that there are probably no simple ways of describing the essential differences between animal language and human language, as of now.

*Bridger:* If you want to look for the crucial difference between human and animal language, you must consider the function of society and the role that society plays in the kind of language that the child acquires. Many workers, including Werner (45), have investigated primitive people, and found, for example, that an Eskimo child or a Lapp child looks at snow and has a different name for it each time, depending on his activity with it, or the kind of situation in which he finds the snow. The word "snow" is absent in this culture and thus the child does not acquire the generalized concept of snow, as such. Only if the child in our culture plays with snow in different situations and the mother keeps saying, "snow," does this word, which is self-signaling, and which the child continually repeats, assume the generalizing and abstracting properties of the concept of snow.

Therefore, I am sure that the animals do not have this society which teaches them a certain word in different contexts to separate the essential from the nonessential object or action in the situation.

*Pribram:* That is, you think animals do not define sets of alternatives out of which events may be chosen?

*Bridger:* What I wanted to do, before going over to this so-called conceptual thinking, was to start off by trying to understand how the animals use the first signal system: Maybe we can show how children start off with words and language, just as animals do and that, for example, the kind of signal these porpoises have is perhaps the same as the kind of signals children have when they are starting off in their development.

*Harlow:* There is presumptive evidence that no animal other than man has the kind of unlearned, call it unconditioned responses, out of which human language evolves. Catherine Hayes (16), in a careful study, found a fragment appearing in the chimpanzee at 3 months and then it disappeared. Thus, we are completely in doubt. No one questions the superiority of man, but as to whether or not a large part of this is that the subhuman animal has failed to learn the kind of unlearned responses is unknown. It would certainly appear that the monkey or the chimpanzee has the intellectual capability to produce a rudimentary kind of language; that is, the monkey, on tests somewhat similar to human mental tests, will do about as well as the lower-grade human imbecile, which certainly attests to a certain amount of language capability. One must recognize that the simple conditional reflex is a technique by which it is not possible, as far as I know, in any way adequately to assess the intellectual capabilities of the subhuman primates. These techniques, I believe, will not differentiate between a cat and a dog and a monkey. Other tests will disclose a very large gulf between the carnivores and secondary primates.

*Lilly:* We spent some time trying to get monkeys to vocalize in order to stimulate their own rewarding systems; in other words, we implanted an electrode in any one of the forward rewarding systems, septal or head of caudate or any of these other places, and then set up a voice cued to food, so, if the monkey cooed, for instance, there would be a short delay and then he would be rewarded with a stimulus in this system. We found quite quickly that they won't do this. We spent about 6 months with two monkeys, trying to get them to do it, and about all we were able to do was get them to coo more frequently during the situations under which they would normally coo, that is, in the expectation of food from the appropriate person.

When we did the same thing with a dolphin, there was no problem whatsoever; in fact, as soon as a rewarding system is hit in the dolphin, extremely complicated vocalization starts immediately. If the reward is now withheld, he will make all sorts of noises, covering a total repertoire that is so much greater than that of the monkey that it is ridiculous to compare the two. The dolphins' creativeness and versatility in the vocal sphere are comparable only to the human, as far as I know. They can whistle, and they can whistle extremely complicated sequences; they can make buzzing noises; they can bark; they can cough. All you have to do is listen to some of these things, and you suddenly realize that you're working with a different magnitude of vocal creativity, a different order. In other words, within the repertoire of these animals, there is a fantastic range of sound patternings, frequency ranges, speech-like bursts and so on, just *au naturelle*, before any training. Then, with training, they will perform vocalizations in a limited area, in order to get a reward. You can get them to specify a certain kind of signal with a definite frequency, of a definite intensity and a definite duration of whistle; for example, if you only reward the dolphin for those three variables, he will experiment within each one of those parameters until he hits the right signal and, from then on, he gets stuck. He is somewhat like a human who is stubborn. Once he has learned that that gives the reward, he won't leave that particular signal at all and will give it to you and expect a reward, and then will not give it to you if you don't give him the reward. It gets to be quite a struggle. Then, unless you excite him emotionally, you can't move him on to another signal, as it were. However, this kind of response cannot be elicited from a monkey. We spent literally months, trying this with macaques.

*Erikson:* What are these three dimensions again, in the dolphin?

*Lilly:* They are the same dimensions that we use. They are intensity, pitch, and duration of the sound.

*Pribram:* An experiment that led to much of the later interest in the dolphin was one at Florida's Marineland. The dolphins were trained to surface for food to Strauss's *Vienna Woods Waltz*, which was played routinely at feeding time, regularly held in the afternoon. One early morning a whole series of Strauss waltzes was played for the dolphins. None of them reacted at all to the waltzes until *Vienna Woods Waltz* was played, at which point a lot of activity could be observed; the dolphins surfaced and jumped near the food platform, although there was no other "feeding stimulus" present. Of course no one has yet discovered a Strauss amongst the dolphins, so we may still cling to our notions of difference between man and beast.

*Brazier:* Would they do that if you transposed the key?

*Lilly:* That hasn't been tried.

*Pribram:* Yes. Wouldn't that be fascinating to try!

*Reynolds:* It would also be interesting to know whether they needed the melody or only a chord sequence or countermelody or something.

*Fremont-Smith:* Quite right. Or rhythm, and how much it could be shortened.

*Pribram:* The dolphin is a special case about which we know little as yet. It is just possible, on the basis of the kind of brain structure owned by this beast, that he *could* do some of the things that human beings do. Dolphins have tremendously large "association" nuclei in the thalamus and comparable projections to cortex.

*Bridger:* There is no doubt, as I was saying before, that just the ability to produce signals does not create this so-called rational speech, as Professor Luria's (31) study on twins indicated. He found that they did not develop consensually validated, societal speech but, rather, they had a language between themselves. They were 5 years old when he found them, and their language was linked with action, linked with practice, and always perceptual, and I am sure they could produce many more sounds than dolphins could, but still, it wasn't—

*Lilly:* Have you ever heard the dolphins?

*Bridger:* They can produce many sounds, probably more than we can. But a child produces many more sounds in the beginning than he does after he develops a formal language. However, these children, in all their psychological tests, performed only at the level of very concrete, synpraxic kind of tactics. Their speech in no way enabled them to acquire any generalizing ability. I am sure Professor Luria can expand on this. Therefore, I do not think that the fact that an animal can make sounds by itself gives it the ability, *per se*, to do with sounds what human beings living in a society can do with sounds.

This, as I say, is a crucial factor. As I mentioned before, some primitive people have a language which is limited, both because of the nature of the culture at the time and the needs of the language for analyzing and dealing with the world. Therefore, the kind of words and the kind of generalizing ability that these words have are very limited, also.

What I wanted to do was to show what the so-called laws of these first signaling system activities are, laws which I think apply initially to all stimuli, whether they come from the outside or are produced by the child or the dolphin.

First, things are associated because of their physical similarity. Also, if dissimilar objects happen to be temporally or spatially contiguous during some activity, they are linked. The objects either signal each other or signal the goal also. This is demonstrated by Wickens' (46) experiment with complex conditioning stimuli. He used a sequence of different types of stimuli followed by reinforcement and found that each component of this complex conditioning stimulus stood for and indicated the next. Of course, Hull (18) has proposed in his reinforcement concept that each signal not only stands for the next one, but also stands for the goal. Since, therefore, both aspects of reinforcement theory can be applied with each signal, objects in the world get linked contiguously or stand for the activity with which they are connected.

Since the animal activity is always related to biological needs, these needs themselves serve as categories for linking things; things which have no obvious — that is, either logical or physical — connection with each other. Since all objects become signals only through activity in this first signaling system, this follows the functioning of von Domarus' (7) principle, that is, the identity of objects through identity of predicate or function. This principle can be applied to many aspects of the activity of the so-called first signaling system. Things become known only as they lead to or are used in the satisfaction of biological requirements. As I said before, Wickens (46) demonstrated that dissimilar stimuli can stand for each other when they are linked during this kind of activity.

*Pribram:* I want to take exception. Satisfaction doesn't have to be just a biological requirement as understood in the "need" sense, but can be obtained in Dr. Harlow's sense also, *e.g.*, that curiosity may be satisfied.

*Bridger:* I call that biological. In fact, I would say, further, and I think Ivanov-Smolensky (19) emphasized this, that the first signaling system in man is not the same as in the animal, since it is determined by social conditions. From the start, its content is determined by the society in which the individual lives, but the form or mechanism is biological. Thus, in an animal world, signals or objects in reality get associated because of physical similarities, contiguity, similarity of function or use, and similarity of biological need or affect or drive or whatever you want to call it. In short, what I am proposing is that the aspects of human cognition that appear to be perceptual or sensory or, so-called primitive or prelogical, are governed by the laws of so-called animal intelligence, first signal system activity.

While, admittedly, this sensory mode of cognition never exists in man in a pure form, isolated from the influence of a second signal system or rational cognition, it shows its influence in many areas of human development, but not necessarily by the same mechanism in each case. While criticizing a strictly hereditarily determined biogenetic approach to psychic development, Gritsenko (15), the Soviet philosopher, whose article was in the collected works translated for this conference, emphasizes that, in certain aspects, there is a repetition in individual human psychic development of characteristic features present in both animal intelligence and human thought at the earliest stages of its historical development.

There is also a similarity between this type of primitive, so-called prelogical thinking and what has been seen in dreams, free associations, brain damage, and schizophrenia. While there is no question but that every one of these similarities occurs under completely different conditions, and thus produces important differences in content, what I propose is that the similarities themselves are due to the functioning of a specific physiological process, the first signaling system.

Before discussing the problem of how humans develop the capacity for symbolic-functioning, conceptual thinking, or second signaling system activity, we must try to specify what we mean by this so-called symbolic function. Cassirer and Langer (5, 23) emphasize that man differs from animals in that he can and does play an active role in determining what value a specific vocal stimulus is to have. The animal does not. The animal does respond to the vocal stimulus or the word, but the animal responds only to the signal qualities of this word. For the human subject, the word has attributes of both signals and symbols. A symbol is a thing the meaning of which is bestowed upon it by those who use it.

Man is a symbol-producing organism. Animals only react to symbols as signals. Man gives signals meaning. Animals react to the meaning of the signals only in relation to the direct activity which links the signals to this activity and not through the consensual validation of the meaning of the signal by society. Sounds can only become words by virtue of a social process.

Man, unlike all other animals, uses signals not only to indicate things, but also to represent them. Most of our words are not used as signals. They are used to talk about things, not to direct our attention toward them. Instead of announcers of things, they are reminders. They are second or substitute signals, for in our present experience they take the place of things that we have perceived in the past or those we may see in the future.

*Lilly:* I would like to ask you what you mean by "social process," when you say that by a social process, words obtain meaning.

*Bridger:* Historical process.

*Lilly:* No, I am talking about an individual human starting with zero language and gradually accumulating one.

*Bridger:* The language itself is developed through a historical process, and is acquired by the child, first through imitation, which is acquiring the words. In this connection, Liyamina (26), another Soviet psychologist, did an interesting experiment, showing that, initially, a baby can acquire a word more easily when it is not connected with action; that is, if you go ahead and teach the baby the word, "ball," and keep on saying "ball" the baby learns to say "ball." If the ball is in front of the baby, he has more difficulty learning to say it than if he is only paying attention to his mother's saying "ball." Once the word is acquired and the baby has the ability to say "ball," he links it with the ball, under the direction of his mother's saying, "This is ball, ball." But if you try to do this simultaneously with presentation of the ball, there will be interference.

At 5½ years of age, the twins in Professor Luria's study had a well-developed language between themselves, and they could communicate their needs while playing with objects and so on. Of course, no one else could understand what they were talking about, and it wasn't a language which was useful in generalizing and abstracting qualities, as witnessed by their psychological test performance (31).

*Kelly:* This is reminiscent of Piaget's use of a 9- or 10-year-old child to interpret the emotional problems of 5- and 6-year-olds. He asked the 9-year-olds to interview them for him and then report what their feelings were, instead of his interviewing the 5- and 6-year-olds directly.

*Bridger:* I think that there are two basic prerequisites for the development of what we call human ability of cognition. One is the biological, which perhaps future investigation will show the dolphin to possess. The other is social, which I think the present evidence shows he does not possess. The biological prerequisite is a self-signaling system, and this self-signaling system has two aspects to its development. The first is the acquisition of the ability to produce these signals through imitating the gestures and speech of the adults and then the repetition of these signals in conjunction with activity with objects.

Piaget (37) also has described these two aspects of learning of speech as separate functions which he calls accommodation and assimilation. The baby learns the words and then learns to connect the words with objects and actions by the repetition of these signals in conjunction with activity with objects.

All this seems to develop on the basis of simple first signaling system activity, and follows the previously described laws of animal-like association. As Professor Luria (31) has described in his study of twins, this primitive self-signaling system is interlocked with action or, as he calls it, is synpraxic. It does not pass the limits of naming objects in the process of direct intercourse with the object. The child is unable to detach the word from the object or the action from the object acted upon.

An animal can also go through a self-signaling process. He can be trained to press a lever which rings a bell, which signals him to press another lever, which puts on a light, and so on, until the reinforcement is given. However, this self-signaling is carried out only through direct action on an object. The animal does not create his own signals, although perhaps the dolphin does.

The child, and probably the animal, by repeated activity with an object in different contexts, develops a somewhat generalized sensory representation of this object, but the mechanism behind the formation of this sensory image is controversial. Some Soviet psychologists such as Zankov (47), Zaporozhets (48), and Elkonin (8), believe it is a product of the orienting-investigative reflex and conditioned trace mechanisms. Piaget (37) believes it is formed through interiorized imitation. Whether animals have these representational images is a difficult question. Human subjects can show conditioned responses without awareness and thus without images.

When a dog responds to a bell with salivation and turning toward the food, does he have an image of the food? Pavlov (35) showed that, when inhibited, the dog salivates to the bell but does not show any movement toward the food. Is that conditioning without awareness? Electrophysiological correlates of these phenomena would be an interesting experiment.

Although it is assumed that the animal does have this capacity for representative imagery, he still cannot attach a self-made signal to this image. An outside signal may evoke this image, but he cannot evoke it himself. The child can signal himself and begin to divorce the representation from the object itself (48).

Piaget (37) holds that intelligence at the sensori-motor level consists in relating present data to past data; he also holds that earlier objects affect present objects only implicitly through the intermediary of action, that is, motor repetition. In cognitive representation, objects not actually perceptible, to which the perceived object is related, are evoked by means of "signifiers" that recall them to mind when they are not actually present. This is the characteristic of the symbolic function, the development of which then involves the differentiation of the "signifier" from the "signified," the signal from what is represented, or, later, the symbol from the object being symbolized.

How does this differentiation of the signifier from the signified occur? Bogoiavlensky (2) says that initially, these words which the child repeats with actions on objects are closely tied with the connected action or object. However, with repetition of the same word in different contexts or actions, a generalization occurs which separates the meaning of the word from the action or the object. This produces what Pavlov called the comprehensive quality of words as compared to signals. The word is connected with many particular objects or actions, subsumed by the general meaning of the word.

The reverse process also occurs, in which different words are used along with similar objects and actions. It is through this mechanism that the essential qualities of objects and actions are separated from nonessential qualities, and the objects themselves get separated from the actions. What we have been talking about here is one aspect of the development of rational cognition—the biological, the capacity for self-signaling. Since it is biological, it is rooted in the same kind of physiological laws that determine animal intelligence, and the language of the child gives good evidence for this. Liublinskaya (25) and Lebedinskaya (24) have shown that children start out responding to the signal-like or impulse qualities of the word, and Professor Luria has given us many examples of how the child reacts to the impulse or motor or signal qualities of the word. In this country, Riess (40) has done some semantic conditioning, and he found that young children show generalizations to homonyms; as they grow older and develop more of a cognitive function, they start generalizing to synonyms and antonyms. Only gradually do they start responding to, or using, the symbolic or conceptual qualities of the word. This gradual development is dependent, on various factors, especially social ones. As mentioned before, the symbolic function of the word comes from the historical development of society.

The crucial historical situation is what I mentioned before. If a culture in which the child is acquiring a language gives the child only specific, concrete words for the specific actions, the generalizing quality of the word will be absent. But in a given culture, what is it that leads to this development of conceptual thinking in the individual? There are some who feel that it is only a problem of training, and many psycholinguists such as Brown (4) feel that if a child is exposed to abstract concepts and generalized words as frequently as he is exposed to specific, concrete words, he will be able to develop abstract thinking rather rapidly. Others, such as Piaget (36), feel that certain experiences with particular objects are necessary before the general concept can be acquired. Perhaps a combined biological-social maturation takes place which enables the child to delay his response to stimuli and thus interpose the self-signaling process.

However, and this is what many psychoanalysts feel, there are certain interactions between the child and his parents which enable the child to neutralize some of the affective qualities of his behavior and thus develop the capacity to acquire a language and secondary process thinking. But, of course, this ability to delay may first be dependent on the creation of language ability to carry out operations internally rather than externally; that is, the language itself may be responsible for the capacity for delay. I think that Professor Luria's study of twins supports the concept that some sort of maturation, independent of this use of language ability, must be taking place, since these children rather rapidly acquired the use of formal thinking. Perhaps something happened during these 5 years, biologically or biosocially, such as family interactions, which enabled the twins to acquire the formal language capacity quickly.

To recapitulate, the child develops his symbolic function on the basis of a self-signaling process which enables him gradually to differentiate the signifier from the signified. He transforms the signal into the symbol. Words are treated more and more by the second signal system processes and less and less by the first signal system processes.

The question is, and I have not mentioned this yet, can we approach this neurophysiologically? After reading some of the recent studies of the electrophysiological correlates of conditioning, I thought perhaps we could approach this problem in a speculative manner.

Both Gastaut (12) and Rowland (41), in their description of the electrophysiological correlates of conditioning, show that the conditioning stimulus and the unconditioned stimulus produce different electrical responses in the area of the neocortex which is the sensory projection of the unconditioned stimulus. Gastaut (12) says that the conditioning stimulus produces a local desynchronization and a secondary evoked response in the unconditioned stimulus cortical area, but no primary evoked response in this area, only in the conditioning stimulus area. The unconditioned stimulus, of course, does produce a primary evoked response in the unconditioned stimulus area.

Malcolm (32) found that during conditioning there was no difference in the responses evoked in the hippocampal region by the conditioning stimulus and the unconditioned stimulus. Rowland also found that during delayed conditioning, while the neocortex shows marked changes during the conditioning stimulus, the hippocampus does not.

It would seem from these experiments that the conditioning stimulus, *i.e.*, the signifier-signal, produces a different electrical response in the neocortex from the unconditioned stimulus, *i.e.*, the signified. However, the hippocampus, and perhaps other limbic as well as reticular regions, produce the same electrical responses with both conditioning stimulus and unconditioned stimulus.

Continuing along the same line, John (20) reported that during the establishment of avoidance conditioning, the hippocampus was activated by the conditioning stimulus, but when the conditioned response was well established and the cat showed no fear in the situation, the electrical response in the cortex became sharper, the response in the reticular activating system lessened, and the response in the hippocampus disappeared. It would seem that the more emotion produced by the stimulus, the greater the hippocampal activity.

I would now like to speculate as to how these neurophysiological phenomena relate to the problem of cognition. It would seem that the neocortex is electrophysiologically able to differentiate signals from what is signaled, but the limbic system cannot. The more the limbic system is activated, the more difficult it will be for the organism to separate the signifier from the signified. In addition, the stronger the emotion aroused by a stimulus, the more likely behavioral activity will be involved, and, also, the more bioelectrical activity will be present in the limbic system. In contrast, the more the individual divorces action from cognition, the less limbic system activity, and the easier the neocortical differentiation of signifier from signified. Also, inhibition of the neocortex will make it difficult to differentiate signifier from signified, or symbol from object symbolized.

As to the evidence in support of this theory, some recent neuropharmacological experiments by K. F. Killam and E. K. Killam (21), Marrazzi (33), Monroe (34), and Purpura (39) suggest that LSD (*d*-lysergic acid diethylamide) and mescaline inhibit cortico-cortical and thalamic recruiting activity with the release and/or simultaneous activation both of specific afferent pathways and of the hippocampal area.

With this inhibition of the neocortex and activation of the limbic system, I postulated that these hallucinogenic drugs would prevent the subject from being able to differentiate the signifier from the signified, or in my experiments (3) the conditioning stimulus from the unconditioned. In a series of experiments,* I found that under the effects of mescaline, animals reacted to the conditioning stimulus as though it were the unconditioned stimulus. When the signal for the shock was given, they howled and squealed as though they were being shocked. This was confirmed by Courvoisier (6) and Sivadjian (42).

Since the conditioning stimulus now had attributes of the unconditioned stimulus, mescaline produced a prolonged resistance to extinction of the conditioned response. This lack of differentiation of signifier from signified occurred primarily in a strong emotional situation, perhaps when hippocampal activity was present. Of interest was the fact that in avoidance conditioning and in mild classical conditioning, with little evidence of fear or other strong emotion, mescaline had the opposite effect, namely rapid extinction. The results of these experiments are illustrated in Figure 196.

As a general approach toward cognition, I would postulate that words and thoughts can have different properties, varying from an abstract logical categorization to the hallucinatory image of the particular object itself.

The word, "chair," can mean the general category of all chairs and can also mean a particular chair. It can even conjure up the hallucinatory image of the chair itself. When a word or idea is used in the general abstract categorical sense, it is called a symbol, and thinking at the rational level of cognition follows the rules of the second signaling system—logical rules. When a thought is dealt with as a particular concrete thing, it is called an image, a signal or a sign, and the rules of

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*This work was supported in part by U.S.P.H.S. Mental Health Career Investigator Grant #M2249.

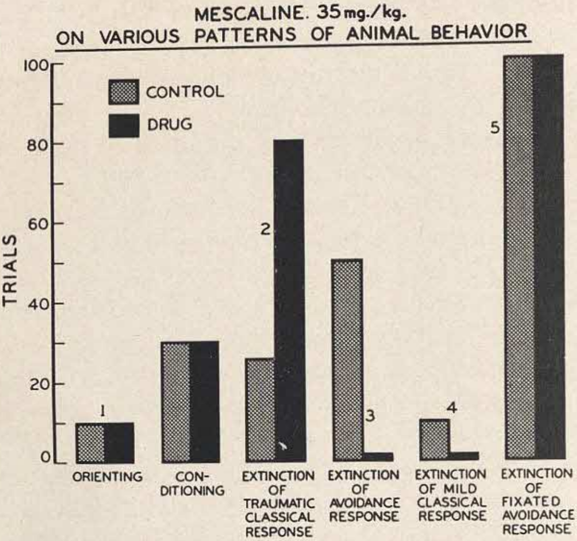

FIGURE 196. These experiments were performed on seventy-two 120-day-old naive Long-Evans hooded rats. Exp. No. 1 indicates that the drug had no effect on the animals' responses to the conditioning stimulus (buzzer) prior to conditioning or reinforcement with electric shock. All the remaining animals had thirty conditioning trials in four different conditioning paradigms. Mescaline was then administered and trials to extinction were measured. Exp. No. 2, classical conditioning with constant reinforcement, indicates that under the effects of the drug the animals continued to respond to the buzzer even though it was not reinforced with shock. The control animals extinguished within twenty-seven trials. In Exp. No. 3, during conditioning, the animals could learn to avoid the shock by turning an activity wheel and thus receive only a few shocks. Exp. No. 4 was identical to No. 2 but the shock was one-tenth as intense. In Exp. No. 5, with each conditioning trial, the animals received a shock in an escape paradigm. The extinction procedure produced "neurotically fixated" avoidance behavior that was not affected by the drug.

thinking at the sensory level of cognition are according to the first signaling system.

Strong emotional experiences tend to shift the cognition process from the rational toward the perceptual or sensory. For example, if one has recently sat on a chair to which a tack was added, the word, "chair," would probably not be thought of as the general category of all chairs, but one would have a tendency to think of or imagine the particular chair associated with the trauma. Any condition which inhibits the neocortex would also shift the cognitive process toward first signaling system activity, or lessen the gap between signifier and signified. Examples of this neocortical inhibition would be sleep, hallucinogenic drugs, sensory deprivation [Heron (17) claimed that the EEG during sensory deprivation resembled that of sleep], sleep deprivation [and this is a study by Armington (1), who said that the EEG resembles sleep], hypnosis, and perhaps schizophrenia, which do not produce the EEG potentials of sleep.

Professor Luria (30) described a study in which chloral hydrate was given to subjects during semantic conditioning. The generalization under chloral hydrate was similar to Riess's (40) study in young children, demonstrating that the generalization was related to the sound of the word, the first signaling system, rather than to the meaning of the word, the second signaling system. Professor Luria (29) also described a similar shift to first signaling system activity in oligophrenia. In addition, he mentioned that when a child has a difficult problem to solve he again starts responding to the so-called impulse aspect or signal quality of the word.

During childhood, the development of the cognitive process is just the reverse—increasing differentiation of the signifier from the signified. I would speculate that there is more neocortical and less limbic system involvement, through more learning from the nondirect or collective social experience and less learning through direct personal emotional experience. As the psychoanalysts would say, this learning occurs through the enlargement of the so-called conflict-free sphere of ego-functioning.

*Lowell:* I would like to make one point that is related to the application of computer techniques to the evaluation of electrophysiological correlates of conditioning and to the problems of sensory physiology. I think it is worth making because often when people hear of computers they shut their minds and conjure up the image of something very large, complicated, unwieldy, and expensive. My point is that this is not necessarily the case. The work that Dr. Brazier and some of her associates have done in the past has led now to the possibility of what she has described as the "poor man's computer." The one that we have constructed (28),* the results of which I will now show, cost considerably less and is simpler to operate than the EEG machine from which it is fed.

The one we have constructed is a special-purpose, on-line analog computer. It has five gates and storage units so that there is not complete freedom of information-gathering, but, based on some of the information that has been gathered with the larger MIT computers, we are able to study evoked auditory responses, with considerable precision and economy of effort, in young pre-language, congenitally deaf children. I would like to show some of the data that we get.

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Figure 197 illustrates evoked auditory responses to monaurally presented auditory clicks. Each subject received 2,048 stimulations at 55 db., but these curves are based on the average of ten subjects.

I present these three curves to show the effect of different repetition rates for the clicks. At 63, 80, and 100 msec., the average evoked waveforms do not change too much. One precaution should be taken in

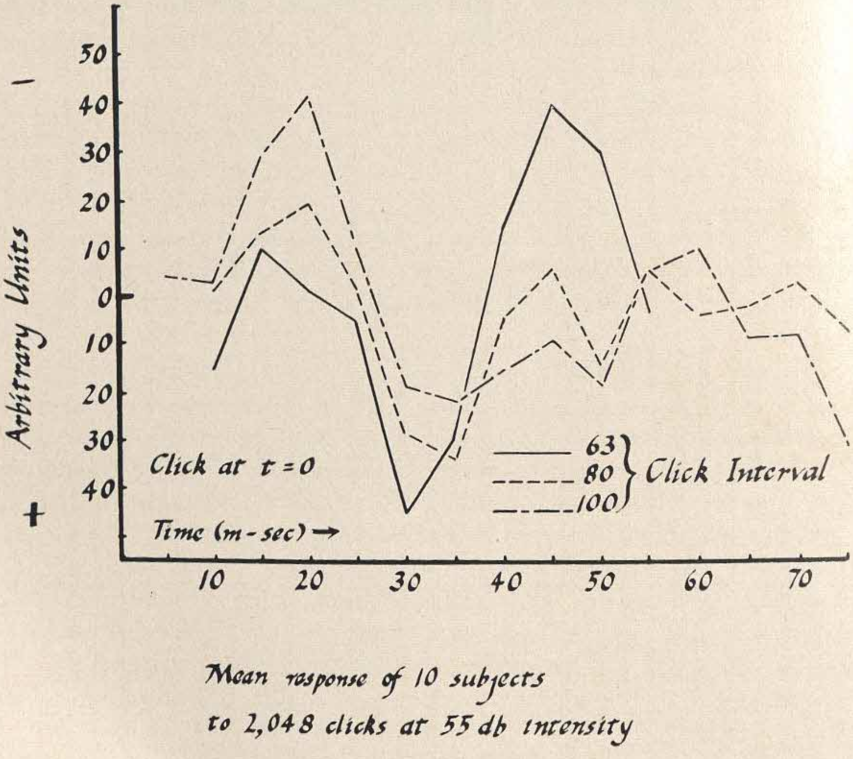


FIGURE 197. Average evoked response curves obtained from ten subjects with 55-db. click presented at 63-, 80-, and 100-msec. intervals. Readings were obtained from 2-msec. gates set at 5-msec. intervals following the click. EEG recordings were from left temporal and left occipital areas with click presented to the right ear. Each subject received 2,048 clicks.

reading this figure: Since the averages are of ten subjects, there is a tendency to pull down the amplitude when we find discrepancies in the individual latencies. This is quite obvious when the group is compared with the individual data. At 80 and 100 msec., there is some hash out beyond 50 msec. that is apparently a function of individual differences in latency.

We then ask ourselves, is this represented bilaterally? Figure 198 deals with (27) this point. This is the average of eleven subjects, 2,048 stimulations at each of the points, with left temporal and left occipital EEG leads and the click presented to both the right and the left ear.

Figure 199 is intended only to show the temporal relations between our data, picked up from gross surface electrodes on the human child,

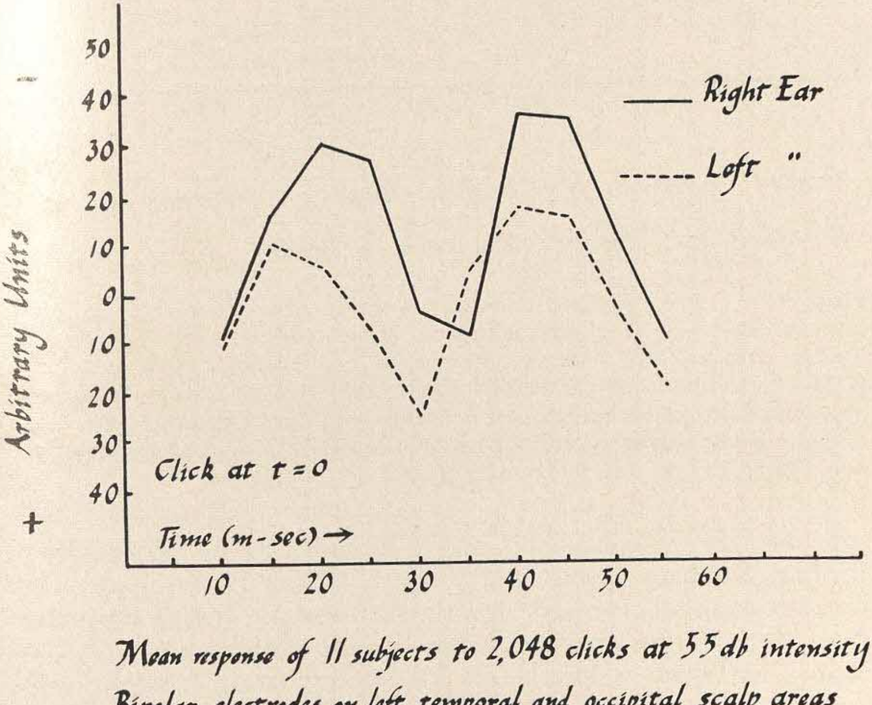
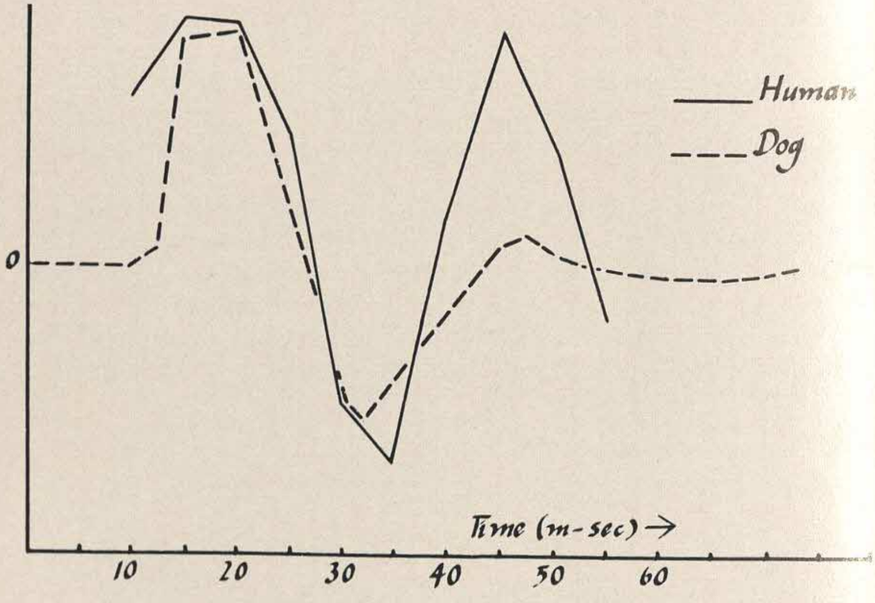


FIGURE 198. Average evoked response of eleven subjects to 55-db. clicks at 80-msec. intervals. Recordings were taken with bipolar EEG leads from left temporal and left occipital areas with the click administered to the right and left ears. Each subject received 2,048 clicks.



Evoked responses of individual subjects. Only time scale is meaningful. Animal data from A. Tunturi.

FIGURE 199. Average evoked response of one subject to 2,048 clicks at 55-db. intensity, delivered at 80-msec. intervals, compared with data presented by Tunturi from the MES auditory cortex of the dog. Polarity of the animal data is reversed for comparison of latency pattern. Only the time scale is the same for both sets of data. Reprinted in part, by permission, from Tunturi, A. R.: Effect of spontaneous activity on afferent response in the MES auditory cortex of the dog. *Am. J. Physiol.* 197, *1141-1146 (1959).*

with the data of Tunturi (44) on the exposed MES auditory cortex in the dog. We have taken a little liberty with Tunturi's data, in that we have reversed polarities, but the temporal relations during this period from 20 to 35 msec., particularly, were quite interesting in their similarity. I think this raises a number of very interesting questions.

We then asked, is this represented all over the cortex, or is it localized in the auditory area? There is a possibility that it was coming from one of the lower centers and was just irradiating out so that by the time we had 2,048 stimulations averaged we might find the same pattern all over the skull. The three curves in Figure 200 represent different pairs

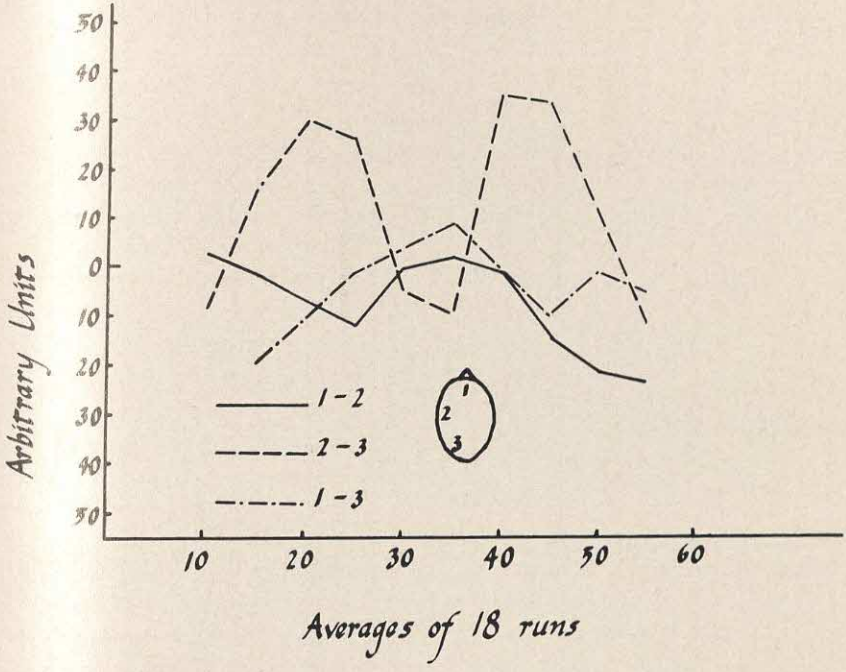


FIGURE 200. Average evoked response curves in a human subject obtained with three electrode placements: left frontal to left temporal, left temporal to left occipital, and left frontal to left occipital. Curves are based on 55-db. clicks delivered at 80-msec. intervals.

of EEG leads. These are bipolar leads from frontal to temporal, from temporal to occipital, and from frontal to occipital. It is evident that the temporal to occipital, which is the standard one we have been using, is the only one which gives us this classic, V-shaped response in the center. The others give a somewhat different response. Dr. Brazier has suggested some additional work that should be done to clarify this picture, but at least the tentative interpretation is that we are picking up something that is fairly well localized in this auditory area. These curves are based on the average of eighteen subjects.

Finally, how does this look in regard to threshold? Figure 201 gives data from a subject with relatively normal hearing in this particular environment. Across the top, there is an indication of subjective awareness. We asked the subject to let us know, by motor signal, whether or not he could hear the burst of clicks before and after the actual test run. Where he could not hear them before or after, we got the kind of

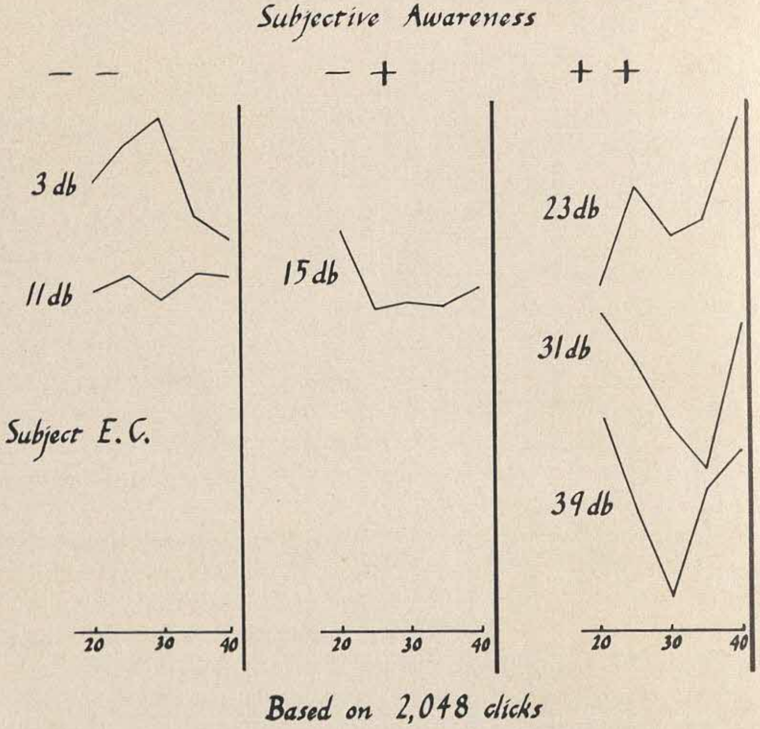


FIGURE 201. Average evoked response curves from a single subject to clicks delivered at differing intensities. Clicks were delivered to the right ear at 80-msec. intervals. EEG recordings taken from the left temporal and left occipital regions. Subjective awareness was indicated by motor response to clicks presented before and after each test run.

pattern shown on the left. At intensities where they could be heard, we got the patterns on the right, which seems to change relatively systematically with intensity.

We feel that this very inexpensive, simple-to-operate technique, applied to the intact human head, which can be used with young children and does not require any special preparation, can potentially lead us to some valuable information on any sort of repetitive sensory stimulus. Any time that a repetitive stimulus can be used, this quite simple, inexpensive computer may have some real value.

*Magoun:* Thank you. Because of Dr. Lowell's experience and interest in language function, he agreed to comment on the latter part of the program, dealing with verbal activity in man. And then I will ask Dr. Pribram to make a closing comment.

*Lowell:* Professor Luria has led us through some experiments that were elegant in their simplicity and their ability to communicate to us the way in which he has approached this very complex area.

It is satisfying to see the way his work has cut across and integrated many of our traditional fields, including child development, neurology, cybernetics, and linguistics. This is most appropriate in view of the multidisciplinary intent of these Macy Conferences, and it is certainly an approach that we will all agree is fruitful if we are to increase our knowledge of human behavior.

It is one thing to describe, as he has, the stages of verbal development in the child and to relate this to the control of behavior, but it is quite another accomplishment to present such a complete set of experiments which illustrate so clearly these stages. The extension of this work to the areas of pathology is most exciting, and one can only await with great interest the development of Professor Luria's proposed research with Dr. Pribram.

I was especially interested in Professor Luria's description of the three stages in the verbal development of the child, and particularly the distinction which he made between the motor-activating and semantic side of speech. This work suggests fruitful areas for investigation for those of us who are interested in the development of verbal behavior in the young, deaf child.

Of great importance, it seems to me, is the emphasis on the way in which verbal behavior interacts with the orienting activity of the organism. Both Professor Luria and Professor Sokolov have made me painfully aware of the way in which many of us have looked upon the orienting reflex as something we wished only to adapt-out or to habituate before we begin our conditioning studies. Professor Luria has focused our attention on a largely neglected area.

To Dr. Bridger, we are all beholden for a most scholarly integration of a great deal of pertinent material on this same problem. It is gratifying to me to know that we are beginning to work intensively on the very young child. I feel that this area has been largely neglected in our own work.

Dr. Bridger made it clear that many workers concerned with cognition have used schemes for classification that are compatible with the Pavlovian description of a first and second signaling system. It is apparent from the discussion that there is less agreement, at least among this group, on the nature of language, and again I am sure that we would all agree with Professor Luria that a whole Macy Conference might be devoted to this topic.

The extension of interest in cognitive activity into the neurophysiological realm, as Dr. Bridger has suggested, is another example of the value of an integrative, multidisciplinary approach to our problems.

*Pribram:* Since the Second Conference on The Central Nervous System and Behavior, some theoretical formulations were accomplished with my colleagues (especially George Miller of Harvard University and Eugene Galanter of the University of Pennsylvania) at the Center for Advanced Study in the Behavioral Sciences. One concerned representational processes in the central nervous system; another dealt with (neural and behavioral) programs or plans; and a third had to do with the cognitive nature of reinforcement.

As of today, last week's theories [*e.g.*, a review of theory in physiological psychology (38)] no longer look very "theoretical." Professor Sokolov gave us exquisitely beautiful evidence to demonstrate that representations are formed in the cerebral cortex during the habituation process. Not only did he show that the representations are formed, but he also detailed something about their multifaceted nature: the temporal time relations involved and how the representations may be modified. The representations have the capability to be self-modifying parts of self-adapting systems. Engineers have been interested in such systems; a neurophysiologist has now demonstrated them to exist in the brain.

Earlier, Dr. Livingston emphasized the importance of something anteceding the motor side responses of an organism similar to the neural organization that takes place with regard to sensory input. And Dr. Doty presented some initial evidence as to how some of these plans (11), as we have called them, could be structured in the central nervous system. Also, Professor Sokolov gave us some additional evidence by showing that his neural model controls not only perception but also action.

With regard to reinforcement, we had the refreshing approach that Professor Luria brought to us. The identification of reinforcement as instructions is an extremely important point. The question of how the frontal lobes and hippocampus function in this process remains to be settled, but convergence of approaches to the problem is remarkable. For instance, your suggestion, Dr. Bridger, that hippocampal activity makes it possible for cognitive process and action to be related through some program or plan (in other words, that the hippocampus is necessary for the execution of plans) is identical with our own view of the matter.

As another example, Professor Luria, with his beautiful demonstrations of the effects of frontal lobe injury in man on the utilization of instruction makes it possible for me to interpret in a similar way some data on discrimination reversal in which monkeys with frontal lesions showed very definite but restricted changes after each reversal.

These are only a few instances where, as a result of this conference, much that was speculative or confusing has become systematic and interpretable. This is very rewarding. In addition, as a result of this gathering, the indications are not only that Professor Luria and I can start to work together, but perhaps some of the others here will work with us. Thus, this promises to have as much future value as did last year's conference.

*Magoun:* I would like to reinforce, I am sure for all of us, how enjoyable it has been to have our three visitors from abroad present at this meeting, and to have communication with them, not only as scientists and as superb expositors of their material, but as charming and friendly colleagues with whom we can enjoy cordial personal associations. It has been most delightful for us all.

## REFERENCES

1. ARMINGTON, J. C., and MITNICK, L. L.: Electroencephalogram and sleep deprivation. *J. Appl. Physiol.* **14**, *247-250 (1959).*
2. BOGOIAVLENSKY, D. N.: The psychology of understanding. *Psychology in the Soviet Union.* Stanford Univ. Press, 1957 (pp. 69-83).
3. BRIDGER, W. H., and GANTT, W. H.: The effect of mescaline on differentiated conditional reflexes. *Am. J. Psychiat.* **113**, *352-360 (1956).*
4. BROWN, R. W.: *Words and Things.* Glencoe, Ill., The Free Press, 1958.
5. CASSIRER, E.: *An Essay on Man.* New Haven, Yale Univ. Press, 1944.
6. COURVOISIER, S.: International symposium on chlorpromazine; pharmacodynamic basis for the use of chlorpromazine in psychiatry. *J. Clin. & Exper. Psychopath.* **17**, *25-37 (1956).*
7. DOMARUS, E. VON: The specific laws of logic in schizophrenia. *Language and Thought in Schizophrenia; Collected Papers.* J. S. Kasanin, Ed. Berkeley and Los Angeles, Univ. of California Press, 1944 (pp. 104-114).
8. ELKONIN, D. B.: The physiology of higher nervous activity and child psychology. *Psychology in the Soviet Union.* Stanford Univ. Press, 1957 (pp. 47-68).
9. FREUD, S.: *Collected Papers.* Vol. IV. London, Hogarth, 1953.
10. FRINGS, H., and FRINGS, M.: The language of crows. *Scient. Am.* **201** *(No. 5), 119-131 (1959).*

11. Galanter, E., Miller, G., and Pribram, K. H.: *Plans and the Structure of Behavior.* New York, Holt, 1960.
12. Gastaut, H.: Some aspects of the neurophysiological basis of conditioned reflexes and behaviour. In: *The Neurological Basis of Behaviour.* G. E. W. Wolstenholme and C. M. O'Connor, Eds. Boston, Little, Brown & Co., 1958 (pp. 255-276).
*13. Georgiyev, F. I.: The problems of the sensory and rational in cognition. *Voprosy Filosofii* (Problems of Philosophy) **1,** *28-41 (1955).*
14. Goldstein, K.: *Language and Language Disturbances: Aphasic Symptom Complexes and Their Significance for Medicine and Theory of Language.* New York, Grune & Stratton, 1948.
*15. Gritsenko, I. I.: Repetition in the process of development. *Voprosy Filosofii* (Problems of Philosophy) **8,** *3-13 (1958).*
16. Hayes, C.: *The Ape in Our House.* New York, Harper, 1951.
17. Heron, W., Doane, B. K., and Scott, T. H.: Visual disturbances after prolonged perceptual isolation. *Canad. J. Psychol.* **10,** *13-18 (1956).*
18. Hull, C. L.: The problem of stimulus equivalence in behavior theory. *Psychol. Rev.* **46,** *9-30 (1939).*
*19. Ivanov-Smolensky, A. G.: Ways and perspectives of the development of the physiology and pathophysiology of the higher nervous activity of the child. *Trudy Instituta vysshey nervnoy deyatel'nosti* (Works of the Institute of Higher Nervous Activity) **2,** *335-346 (1956).*
20. John, E. R.: Discussion in: *The Central Nervous System and Behavior.* M. A. B. Brazier, Ed. Trans. First Conf. New York, Josiah Macy, Jr. Foundation, 1958 (pp. 333-347).
21. Killam, K. F., and Killam, E. K.: The action of lysergic acid diethylamide on central afferent and limbic pathways in the cat. *J. Pharmacol. & Exper. Therap.* **116,** *35-36 (1956).*
22. Koehler, O.: The ability of birds to "count." *Bull. Animal Behav.* **9,** *41-45 (1951).*
23. Langer, S. K.: *Philosophy in a New Key . . .* Cambridge, Mass., Harvard Univ. Press, 1942.
*24. Lebedinskaya, Y. I., and Polyakova, A. G.: Certain age modifications of the interaction of the first and second signal systems in children two to seven years of age. *Voprosy Psikhologii* (Problems of Psychology) **3** *(No. 1), 53-60 (1957).*
*25. Liublinskaya, A. A.: The development of children's speech and thought. *Psychology in the Soviet Union.* Stanford Univ. Press, 1957 (pp. 197-204).
*26. Liyamina, G. M.: Mechanism by which children master pronunciation during the second and third year. *Voprosy Psikhologii* (Problems of Psychology) **4** *(No. 6), 119-130 (1958).*
27. Lowell, E. L., and Troffer, C. I.: Auditory threshold detection by temporal evannation. *J. Speech & Hearing Res.* (In press).

28. Lowell, E. L., Troffer, C. I., Warburton, E., and Rushford, G.: Temporal evannation: a new approach in diagnostic audiology. *J. Speech & Hearing Disorders* (In press).
29. Luria, A. R.: Directive function of speech in development and dissolution. *Word* **15** *(No. 2), 341-352 (1959).*
30. Luria, A. R., and Vinogradova, O. S.: An objective investigation of the dynamics of semantic systems. *Brit. J. Psychol.* **50,** *89-105 (1959).*
31. Luria, A. R., and Yudovich, F. I.: *Speech and the Development of Mental Processes in the Child.* Staples Press, 1959.
32. Malcolm, J. L.: The electrical activity of cortical neurones in relation to behaviour, as studied with microelectrodes in unrestrained cats. In: *The Neurological Basis of Behaviour.* G. E. W. Wolstenholme, and C. M. O'Connor, Eds. Boston, Little, Brown, 1958 (pp. 295-302).
33. Marrazzi, A. S., and Hart, E. R.: Relationship of hallucinogens to adrenergic cerebral neurohumors. *Science* **121,** *365-367 (1955).*
34. Monroe, R. R., Heath, R. G., Mickle, W. A., and Llewellyn, R. C.: Correlation of rhinencephalic electrograms with behavior. A study on humans under the influence of LSD and mescaline. *EEG Clin. Neurophysiol.* **9,** *623-642 (1957).*
35. Pavlov, I. P.: Conditioned reflexes and psychiatry. *Lectures on Conditioned Reflexes.* Vol. II. (Translated and edited by W. H. Gantt) New York, Internat. Publishers, 1928-1941.
36. Piaget, J.: *The Psychology of Intelligence.* London, Routledge & Paul, 1950.
37. ———: *Play, Dreams, and Imitation in Childhood . . .* New York, Norton, 1951.
38. Pribram, K. H.: A review of theory in physiological psychology. *Ann. Rev. Psychol.* **11,** *1-40 (1960).*
39. Purpura, D. P.: Electrophysiological analysis of psychotogenic drug action; effect of LSD on specific afferent systems in cat. *A.M.A. Arch. Neurol. & Psychiat.* **75,** *122-131 (1956).*
40. Riess, B. F.: Genetic changes in semantic conditioning. *J. Exper. Psychol.* **36,** *143-152 (1946).*
41. Rowland, V.: Differential electroencephalographic response to conditioned auditory stimuli in arousal from sleep. *EEG Clin. Neurophysiol.* **9,** *585-594 (1957).*
42. Sivadjian, J.: Étude pharmacologique d'un réflexe conditionné. *Compt. rend. Acad. sc.* **199,** *884-886 (1934).*
43. Sullivan, H. S.: *The Interpersonal Theory of Psychiatry.* New York, Norton, 1953.
44. Tunturi, A. R.: Effect of spontaneous activity on afferent response in the MES auditory cortex of the dog. *Am. J. Physiol.* **197,** *1141-1146 (1959).*
45. Werner, H.: *Comparative Psychology of Mental Development.* New York, Internat. Univ. Press, 1957.

46. WICKENS, D. D.: Conditioning to complex stimuli. *Am. Psychol.* 14, *180-188 (1959).*
47. ZANKOV, L. V.: The theory of memory. *Psychology in the Soviet Union.* Stanford Univ. Press, 1957 (pp. 152-163).
*48. ZAPOROZHETS, A. V.: Origin and development of conscious control of movements in man. *Voprosy Psikhologii* (Problems of Psychology) 4 *(No. 1), 24-36 (1958).*

---

*An English translation of the papers starred is included in *The Central Nervous System and Behavior: Selected Translations from the Russian Medical Literature* (in two volumes), which was precirculated to members of the conference by the U. S. Department of Health, Education, and Welfare and distributed to medical schools in the United States and Canada.

# TRANSLATIONS FROM THE RUSSIAN MEDICAL LITERATURE

In preparation for this conference several journals from the USSR were reviewed for the period 1956-58, selections being mostly from the following seven: Biophysics, Pavlov Journal of Higher Nervous Activity, Korsakov Journal of the USSR, Problems of Psychology, Problems of Philosophy, and the Sechenov Journal of Physiology.

English translations of seventy articles, selected for their relevance to the subject matter of the conference, were made available to the participants. Copies of these translations have been distributed to the libraries of all medical schools in the United States and Canada in a volume entitled *The Central Nervous System and Behavior*, compiled by the U. S. Department of Health, Education, and Welfare, Public Health Service, 1960.

The list of articles appears below:

ANTONOV, N. P.: Specific nature of the individual consciousness of man as the highest degree of mental development. *Problems of Psychol.* 4 *(No. 6), 79-87 (1958).*

ASLANOV, A. S.: Problems connected with joint activity of the first and second signal system in normal and pathological states. *J. Higher Nerv. Act.* 8 *(No. 1), 192-202 (1958).*

BABKIN, P. S.: The establishment of reflex activity in early postnatal life. *Sechenov Physiol. J. USSR* 44 *(No. 10), 922-927 (1958).*

BIRIUKOV, D. A., VEDIAEV, F. P., ZAGORUL'KO, T. M., and KARAMIAN, A. I.: A substantial contribution to the development of comparative physiology. In Principles of Comparative Physiology. *The Comparative Physiology of the Nervous System.* Vol. II. Moscow, Academy of Sciences Press, 1957.

BIRYUKOV, D. A.: Landmarks in the development of the theory of reflex activity. *Sechenov Physiol. J. USSR* 44 *(No. 1), 77-82 (1958).*

BRAUN, A. A., and MIKHAILOV, V. P.: A. A. Zavarzin and N. G. Khlopin's theories of tissue evolution and the problem of their creative synthesis. *Arch. Anat., Histol., & Embryol.* 35 *(No. 3), 8-18 (1958).*

BRINKS, Z. N.: Experimental investigations of the typological characteristics of the higher nervous activity in school age children. *Works Inst. Higher Nerv. Act.* 2, *149-174 (1956).*

CHLENOV, L. G.: Cybernetics in neurology. *J. Neuropath. & Psychiatry* 63 *(No. 10), 1259-1264 (1958).*

CHRELASHVILI, N. V.: Critical moment in the psychic development of the child. *Problems of Psychol.* 4 *(No. 4), 105-115 (1958).*

DASHKOVSKAYA, V. S.: The first conditioned reactions in newborn infants under normal and in certain pathological conditions. *J. Higher Nerv. Act.* 3 *(No. 2), 247-259 (1953).* (Moscow)

DAVYDOVA, A. N.: Experimental psychological investigation of manifestations of the will of young people. *Psychol. & Pedagogy* 214 *(No. 9), 29-44 (1956).*

FEDEYEVA, V. K.: The peculiarities of the interaction between the first and second signaling systems in the course of formation of conditioned reflexes to complex stimuli in children. *J. Higher Nerv. Act.* 3, *28-42 (1951).*

FRANK, G. M., and ENGEL'GARDT, V. A.: The role of physics and chemistry in the investigation of biological problems. *Problems of Philos.* 9, *58-72 (1958).* (Moscow)

FROLOV, I. T.: Determinism and teleology. *Prolems of Philos.* 2, *35-49 (1958).*

GRITSENKO, I. I.: Repetition in the process of development. *Problems of Philos.* 8, *3-13 (1958).*

HAHN, P.: The development of heat polypnoea in pups. *Sechenov Physiol. J. USSR* 44 *(No. 1), 23-28 (1958).*

IANUSH, I. M.: Effect of neurosis-producing influences on the conditioned reflexes of rabbits during pregnancy and lactation and on the growth rates of their young. *Sechenov Physiol. J. USSR* 44 *(No. 12), 1131-1136 (1958).*

INCHINA, V. I.: Reacting to water excess and water deficiency in the early postnatal period. *Material on Evolutionary Physiology* 2, *160-171 (1957).*

IVANOV-SMOLENSKY, A. G.: Ways and perspectives of the development of the physiology and pathophysiology of the higher nervous activity of the child. *Works Inst. Higher Nerv. Act.* 2, *335-346 (1956).*

KABANOVA-WELLER, YE. N.: Formation of space perception and spatial concepts in children. *Problems of Psychol.* 4 *(No. 3), 161-167 (1958).*

KARAMYAN, A. I.: Some mechanisms of physiologico-morphological evolution of the higher divisions of the central nervous system in vertebrates. *Material on Evolutionary Physiology* 2, *86-101 (1957).*

KASATKIN, N. I.: Early conditioned reflexes in the child. *J. Higher Nerv. Act. im. I. P. Pavlov* 2 *(No. 4), 572-581 (1952).*

KASATKIN, N. I., MIRZOYANTS, N. S., and KHOKHITVA: Oriented conditioned reflexes in infants during the first year of life. *J. Higher Nerv. Act.* 3 *(No. 2), 192-202 (1953).*

KHAVKINA, N. N.: Functional characteristics of centers in relation to the formation of a dominant state in man. *Sechenov Physiol. J. USSR* 44 *(No. 9), 873-881 (1958).*

KHUDOROZHEVA, A. T.: Role of the cerebellum in the development of the functions of skeletal muscles in ontogenesis. *Material on Evolutionary Physiology* 1, *333-348 (1956).*

KIRZON, M. V., and KLIMOVITSKII, V. YA.: The problem of so-called "spontaneous" excitations of the central nervous system. *Biophysics* 3 *(No. 1), 108-110 (1958).*

KNORRE, A. G.: Forty years of Soviet embryology. *Arch. Anat., Histol., & Embryol.* 35 *(No. 2), 3-16 (1958).*

KOSMARSKAYA, YE. N.: Development of area 17 of the cerebral cortex in humans during the second half of intrauterine life. *Arch. Anat., Histol., & Embryol.* 35 *(No. 2), 30-38 (1958).*

Krasil'nikova, V. I.: Histochemistry of brain phosphatase in rabbits during ontogenesis. *Arch. Anat., Histol., & Embryol.* 35 *(No. 3), 69-72 (1958).*

Kremyansky, V. I.: Certain peculiarities of organisms as a "system" from the point of view of physics, cybernetics and biology. *Problems of Philos.* 8, *97-107 (1958).*

Krylov, O. A.: Relationship between changes in higher nervous activity and the bromine content of the blood in monkeys (*Papio Hamadryas*) in the course of ontogenesis. *J. Higher Nerv. Act.* 8 *(No. 3), 358-365 (1958).*

Lapshin, O. V.: Materialist theory of reflection and the theory of development of living matter. *Problems of Philos.* 4, *78-87 (1958).*

Lebedinskaya, Ye. I., and Polyakova, A. G.: Certain age modifications of the interaction of the first and second signal system in children two to seven years of age. *Problems of Psychol.* 3 *(No. 1), 53-60 (1957).*

Linkovskii, G. B.: The brain as a system of autonomic "memory." *Biophysics* 3 *(No. 4), 385-390 (1958).*

Liyamina, G. M.: Mechanism by which children master pronunciation during the second and third year. *Problems of Psychol.* 4 *(No. 6), 119-130 (1958).*

Luria, A. R.: Experimental analysis of the development of voluntary action in children. *XV Internat. Congr. Psychol., 1958.*

———: The role of speech in child development. *Problems of Psychol.* 4 *(No. 5), 3-17 (1958).*

Luria, A. R., and Vinogradova, O. S.: An objective investigation of the dynamics of semantic systems. *Academy of Pedagogical Sciences of R.S.F.S.R. and University of Moscow.*

Makarov, P. V.: Recent data on the structure and properties of the cell nucleus. *Arch. Anat., Histol., and Embryol.* 35 *(No. 6), 3-21 (1958).*

Marushevsky, M.: On the interaction of the two signal systems in orientation reactions. *Problems. of Pscyhol.* 3 *(No. 1), 78-87 (1957).*

Mikhaleva, O. A.: Influences from the splanchnic nerve on the secretory functions of adrenal glands in newborn animals. *Material on Evolutionary Physiology* 1, *213-218 (1956).*

———: Mechanisms producing inhibitory influences on the cardio-vascular activity in animals (puppies) during their ontogenetic development. *Material on Evolutionary Physiology* 1, *246-252 (1956).*

———: Vasomotor influences from the cephalic portion of the vagosympathetic trunk severed in the neck region in newborn animals (puppies). *Material on Evolutionary Physiology* 1, *219-230 (1956).*

Morozov, V. M.: Depth psychology and psychiatry. *J. Neuropath. & Psychiatry* 58 *(No. 11), 1399-1406 (1958).*

Naroditskaya, G. D.: Complex dynamic structure in children of different ages. *Works Inst. Higher Nerv. Act.* 2, *129-135 (1956).*

Nikitina, G. M.: Interrelations in the development of orientation reactions and conditioned motor reactions in ontogenesis. *J. Higher Nerv. Act.* 4 *(No. 3), 406-414 (1954).*

Nikolenko, K. A.: Ontogenetic changes in the reflex regulation of renal function. *Material on Evolutionary Physiology* 2, *151-159 (1957).*

Norina, O. A.: Effect of diuretics in the early postnatal period. *Material on Evolutionary Physiology* 2, *172-180 (1957).*

NORKINA, L. N.: The production of experimental neurotic states in the lower ages. *J. Higher Nerv. Act.* **8** *(No. 1), 56-63 (1958).*

NOVLYANSKAYA, K. A.: One of the forms of prolonged pathological reactions in puberty (anorexia nervosa in adolescents). *J. Neuropath. & Psychiatry* **58** *(No. 7), 861-866 (1958).*

NUZHDIN, N. I.: Methodological problems in contemporary genetics. *Problems of Philos.* **8,** *82-96 (1958).*

PANCHENKO, L. F.: Protein turnover in various parts of the central nervous system in relation to age. *Sechenov Physiol. J. USSR* **44** *(No. 3), 243-248 (1958).*

PEIMER, I. A.: Local electrical responses in the cerebral cortex of man and their relationship to generalized reactions in the process of conditioned reflex activity. *Sechenov Physiol. J. USSR* **44** *(No. 9), 829-838 (1958).*

PETROV, D. F.: Philosophical problems in the theory of the material basis of heredity. *Problems of Philos.* **7,** *102-112 (1958).*

PORTUGALOV, V. V.: Topography of proteins in the central nervous system. *J. Neuropath. & Psychiatry* **58** *(No. 6), 641-649 (1958).*

RASPOPOV, P. P.: Phasic states of excitability of the cerebral cortex as related to certain individual psychological characteristics of students. *Problems of Psychol.* 4 *(No. 2), 23-37 (1958).*

ROZHE, A., VORONIN, L. G., and SOKOLOV, YE. M.: Electroencephalographic research on temporary association with dampening of the orientation reflex in man. *J. Higher Nerv. Act.* **8** *(No. 1), 3-16 (1958).*

SEREDINA, M. I.: Selective irradiation of extinguishing inhibition at different age levels. *Works Inst. Higher Nerv. Act.* 2, *88-98 (1956).*

SHAMARINA, N. M.: Readjustment of innervation relationships in the central nervous system resulting from transplantation of antagonist muscles. *Sechenov Physiol. J. USSR* 44 *(No. 11), 1040-1048 (1958).*

SHEIVEKHMAN, B. E.: Methods of fixing speech habits developed in deaf-mute children practically deprived of hearing. *Material on Evolutionary Physiology* 2, *186-195 (1957).*

SHIPKOVENSKY, N. S.: The "ink blot" method in determining the characteristics of the signal systems in persons of different temperaments. *J. Neuropath. & Psychiatry* **58** *(No. 11), 1326-1332 (1958).*

SUKHOBSKAYA, G. S.: Development of automatic performance of mental activities. *Problems of Psychol.* 4 *(No. 3), 74-86 (1958).*

TAGIYEV, SH. K.: Synthesis of two different motor conditioned reflexes into a chain of movement in fishes, pigeons and rabbits. *J. Higher Nerv. Act.* **8** *(No. 3), 431-436 (1958).*

TROITSKAYA, S. A.: Rate of maturing of the spinal reflex arcs in rabbits. *Arch. Anat., Histol., & Embryol.* **35,** *(No. 6), 52-57 (1958).*

TURBIN, N. V.: Philosophical problems in contemporary genetics. *Problems of Philos.* 2, *112-127 (1958).*

UMANSKY, L. I.: Experimental study of typological characteristics of the nervous system in children (from play material). *Problems of Psychol.* 4 *(No. 1), 184-190 (1958).*

YAROSHEVSKY, M. G.: Psychology and the concept of the reflex. *Problems of Psychol.* 4 *(No. 6), 66-78 (1958).*

ZAPOROZHETS, A. V.: Origin and development of conscious control of movements in man. *Problems of Psychol.* 4 *(No. 1), 24-36 (1958).*

ZHUKOV-VEREZHNIKOV, N. N., and PEKHOV, A. P.: Genetics of microorganisms and present-day views on heredity. *Problems of Philos.* 6, *127-138 (1958).*

ZURABASHVILI, A. D.: Cybernetics and some problems in psychiatry. *J. Neuropath. & Psychiat.* 63 *(No. 10), 1264-1268 (1958).*

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